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These are articles that pertain to the domain of HIV and Aging.

Most studies done outside the USA are not included unless pertinent.

Abstract Background Aged individuals respond poorly to vaccination and have a higher risk of contracting infections in comparison to younger individuals; whether age impacts on the composition and function of B cell subpopulations relevant for immune responses is still controversial. It is also not known whether increased age during HIV-1 infection further synergizes with the virus to alter B cell subpopulations. In view of the increased number of HIV-1 infected patients living to high age as a result of anti-retroviral treatment this is an important issue to clarify. Results In this work we evaluated the distribution of B cell subpopulations in young and aged healthy individuals and HIV-1 infected patients, treated and naïve to treatment. B cell populations were characterized for the expression of inhibitory molecules (PD-1 and FcRL4) and activation markers (CD25 and CD69); the capacity of B cells to respond to activation signals through up-regulation of IL-6 expression was also evaluated. Increased frequencies of activated and tissue-like memory B cells occurring during HIV-1 infection are corrected by prolonged ART therapy. Our findings also reveal that, in spite of prolonged treatment, resting memory B cells in both young and aged HIV-1 infected patients are reduced in number, and all memory B cell subsets show a low level of expression of the activation markers CD25. Conclusions The results of our study show that resting memory B cells in ART-treated young and aged HIV-1 infected patients are reduced in number and memory B cell subsets exhibit low expression of the activation marker CD25. Aging per se in the HIV-1 infected population does not worsen impairments initiated by HIV-1 in the memory B cell populations of young individuals.


BACKGROUND: Chronic inflammation and immune activation occur in both HIV infection and normal aging and are associated with inflammatory disease. However, the degree to which HIV influences age-related innate immune changes, and the biomarkers which best reflect them, remains unclear. METHODS AND RESULTS: We measured established innate immune aging biomarkers in 309 individuals including 88 virologically suppressed (VS) and 52 viremic (viral load </= and >50 copies per milliliter, respectively) HIV-positive individuals. Levels of soluble (ie, CXCL10, soluble CD163, neopterin) and cellular (ie, proportions of inflammatory CD16 monocytes) biomarkers of monocyte activation were increased in HIV-positive individuals and were only partially ameliorated by viral suppression. Viremic and VS HIV-positive individuals show levels of age-related monocyte activation biomarkers that are similar to uninfected controls aged 12 and 4 years older, respectively. Viremic HIV infection was associated with an accelerated rate of change of some monocyte activation markers (eg, neopterin) with age, whereas in VS individuals, subsequent age-related changes occurred at a similar rate as in controls, albeit at a higher absolute level. We further identified CXCL10 as a robust soluble biomarker of monocyte activation, highlighting the potential utility of this chemokine as a prognostic marker. IMPLICATIONS: These findings may partially explain the increased prevalence of inflammatory age-related diseases in HIV-positive individuals and potentially indicate the pathological mechanisms underlying these diseases, which persist despite viral suppression.

The prevalence of the metabolic syndrome, a cluster of cardiovascular risk factors associated with obesity and insulin resistance, is dramatically increasing in Western and developing countries. This disorder consists of a cluster of metabolic conditions, such as hypertriglyceridemia, hyper-low-density lipoproteins, hypo-high-density lipoproteins, insulin resistance, abnormal glucose tolerance and hypertension, that-in combination with genetic susceptibility and abdominal obesity—are risk factors for type 2 diabetes, vascular inflammation, atherosclerosis, and renal, liver and heart diseases. One of the defects in metabolic syndrome and its associated diseases is excess of reactive oxygen species. Reactive oxygen species generated by mitochondria, or from other sites within or outside the cell, cause damage to mitochondrial components and initiate degradative processes. Such toxic reactions contribute significantly to the aging process. In this article we review current understandings of oxidative stress in metabolic syndrome related disease and its possible contribution to accelerated senescence. [ABSTRACT FROM AUTHOR]


PURPOSE OF REVIEW: This article explores new data from recent studies addressing the role of coinfections in immune activation in HIV-1-infected patients, with a focus on immune reconstitution inflammatory syndrome (IRIS), an aberrant inflammatory response occurring shortly after antiretroviral therapy (ART) initiation. RECENT FINDINGS: Chronic HIV infection is associated with several coinfections that contribute to immune activation in various settings including early after ART initiation in the most noticeable form of IRIS and also in chronic-treated infection, with chronic viral infections like cytomegalovirus and hepatitis C or hepatitis B virus contributing to immune activation and also morbidity and mortality. Expanding on older studies, the role of T cells in IRIS has been further elucidated with evidence of more pronounced effector activity in patients with IRIS that may be leading to excessive tissue disorder. Newer studies are also continuing to shed light on the role of myeloid cells as well as the contribution of antigen load in IRIS. In addition, preliminary data are beginning to suggest a possible role of inflammasome formation in IRIS. In cryptococcal IRIS, the role of activated immune cells (T cell and myeloid) and biomarkers were evaluated in more detail at the site of infection (cerebrospinal fluid). Finally, important differences of patients developing IRIS versus those who die from tuberculosis despite ART initiation were reported, a distinction that may have important implications for participant selection in studies aiming to prevent IRIS with immunosuppressive agents. SUMMARY: Better understanding of the role of opportunistic infections at ART initiation and IRIS pathogenesis will assist in improved strategies for prevention and treatment. The long-term consequences of IRIS remain unclear. Chronic viral coinfections with herpesviruses and hepatitis C virus are important factors in persistent immune activation in chronic-treated HIV.


OBJECTIVE: To evaluate the association of plasma inflammatory biomarkers with MetS in an older population of treated HIV-infected (HIV+) as compared to age-matched HIV-negative (HIV-) adults. DESIGN: Retrospective observational study. METHODS: Plasma concentrations of complement component 3 (C3), cystatin C, fibroblast growth factor 1, interleukin 6, oxidized LDL, soluble RAGE, soluble CD163, soluble CD14, and osteopontin were measured in 79 HIV+ participants on combination antiretroviral treatment (cART) with a suppressed HIV viral load and 47 HIV- participants with a median age of 59 (range 50 to 79). Outcomes were individual MetS components (hypertension, type II diabetes, dyslipidemia, and obesity) and MetS. Covariates were screened for inclusion in multivariable models. Odds ratios are reported per 50 mg/dL increase in C3. RESULTS: In the HIV+ group, higher C3 levels were associated with MetS (OR 3.19, p=0.004), obesity (OR 2.02, p=0.01), type II diabetes (OR 1.93, p=0.02) and
at a trend level with dyslipidemia (OR 1.87, p=0.07) and hypertension (OR 1.66, p=0.09). C3 levels were significantly higher in HIV+ participants with MetS compared to those without MetS (p=0.002). C3 was higher among HIV+ patients with three or four MetS components as compared to those with one or two (p=0.04) and those with none (p=0.002). No associations were found between C3 and the outcomes for HIV- participants. CONCLUSIONS: C3 is strongly associated with both MetS and MetS components in an older HIV+ sample on cART compared to HIV- controls. C3 warrants further investigation as a marker of cardiometabolic risk among persons aging with HIV.


Antiretroviral therapy has increased the life span of HIV+ individuals; however, HIV-associated neurocognitive disorder (HAND) occurrence is increasing in aging HIV patients. Previous studies suggest HIV infection alters autophagy function in the aging CNS and HIV-1 proteins affect autophagy in monocyte-derived cells. Despite these findings, the mechanisms leading to dysregulated autophagy in the CNS remain unclear. Here we sought to determine how HIV Tat dysregulates autophagy in neurons. Tat caused a dose-dependent decrease in autophagosome markers, microtubule-associated protein-1 light chain beta II (LC3II), and sequestosome 1(SQSTM1), in a membrane-enriched fraction, suggesting Tat increases autophagic degradation. Bafilomycin A1 increased autophagosome number, LC3II, and SQSTM1 accumulation; Tat cotreatment diminished this effect. Tat had no effect when 3-methyladenine or knockdown of beclin 1 blocked early stages of autophagy. Tat increased numbers of LC3 puncta and resulted in the formation of abnormal autophagosomes in vitro. Likewise, in vivo studies in GFAP-Tat tg mice showed increased autophagosome accumulation in neurons, altered LC3II levels, and neurodegeneration. These effects were reversed by rapamycin treatment. Tat colocalized with autophagosome and lysosomal markers and enhanced the colocalization of autophagosome with lysosome markers. Furthermore, co-IP studies showed that Tat interacts with lysosomal-associated membrane protein 2A (LAMP2A) in vitro and in vivo, and LAMP2A overexpression reduces Tat-induced neurotoxicity. Hence, Tat protein may induce autophagosome and lysosome fusion through interaction with LAMP2A leading to abnormal neuronal autophagy function and dysregulated degradation of critical intracellular components. Therapies targeting Tat-mediated autophagy alterations may decrease neurodegeneration in aging patients with HAND.


Although the use of antiretroviral therapy (ART) has proven highly effective in controlling and suppressing HIV1 replication, the persistence of latent but replication-competent proviruses in a small subset of CD4 + memory T cells presents significant challenges to viral eradication from infected individuals. Attempts to eliminate latent reservoirs are epitomized by the ‘shock and kill’ approach, a strategy involving the combinatorial usage of compounds that influence epigenetic modulation and initiation of proviral transcription. However, efficient regulation of viral premRNA splicing through manipulation of host cell splicing machinery is also indispensable for HIV1 replication. Interestingly, aberrant alternative splicing of the LMNA gene via the usage of a cryptic splice site has been shown to be the cause of most cases of Hutchinson–Gilford progeria syndrome (HGPS), a rare genetic condition characterized by an accelerated aging phenotype due to the accumulation of a truncated form of lamin A known as progerin. Recent evidence has shown that inhibition of the splicing factors ASF/SF2 (or SRSF1) and SRp55 (or SRSF6) leads to a reduction or an increase in progerin at both the mRNA and protein levels, respectively, thus altering the LMNA premRNA splicing ratio. It is also well-established that during the latter stages of HIV1 infection, an increase in the production and nuclear export of unspliced viral mRNA is indispensable for efficient HIV1 replication and that the
presence of ASF/SF2 leads to excessive viral premRNA splicing and a reduction of unspliced mRNA, while the presence of SRp55 inhibits viral premRNA splicing and aids in the generation and translation of unspliced HIV1 mRNAs. The splicing factor associated protein and putative mitochondrial chaperone p32 has also been shown to inhibit ASF/SF2, increase unspliced HIV1 viral mRNA, and enhance mitochondrial DNA replication and oxidative phosphorylation. It is our hypothesis that activation of AMPK, a master regulator of cellular metabolism which has been shown to activate PKCθ and is essential for T cell activation, may and latency in HIV1 infected T cells. AMPK activating compounds including metformin and resveratrol may thus embody a novel treatment paradigm linking the pathophysiology of HGPS with that of HIV1 latency.


Aging is accompanied by many physiological changes including those in the immune system. These changes are designated as immunosenescence indicating that age induces a decrease in immune functions. However, since many years we know that some aspects are not decreasing but instead are increasing like the pro-inflammatory activity by the innate immune cells, especially by monocytes/macrophages. Recently it became evident that these cells may possess a sort of memory called trained memory sustained by epigenetic changes occurring long after even in the absence of the initiator aggressor. In this review we are reviewing evidences that such changes may occur in aging and describe the relationship between inflamm-aging and immunosenescence as an adaptation/remodelling process leading on one hand to increased inflammation and on the other to decreased immune response (immune-paralysis) mastered by the innate immune system. These changes may collectively induce a state of alertness which assure an immune response even if ultimately resulting in age-related deleterious inflammatory diseases.


Residents of distressed urban areas suffer early aging-related disease and excess mortality. Using a community-based participatory research approach in a collaboration between social researchers and cellular biologists, we collected a unique data set of 239 black, white, or Mexican adults from a stratified, multistage probability sample of three Detroit neighborhoods. We drew venous blood and measured telomere length (TL), an indicator of stress-mediated biological aging, linking respondents' TL to their community survey responses. We regressed TL on socioeconomic, psychosocial, neighborhood, and behavioral stressors, hypothesizing and finding an interaction between poverty and racial-ethnic group. Poor whites had shorter TL than nonpoor whites; poor and nonpoor blacks had equivalent TL; and poor Mexicans had longer TL than nonpoor Mexicans. Findings suggest unobserved heterogeneity bias is an important threat to the validity of estimates of TL differences by race-ethnicity. They point to health impacts of social identity as contingent, the products of structurally rooted biopsychosocial processes.


INTRODUCTION: HIV infection and its therapy which can affect their aerobic capacity and health-related quality of life of patients. OBJECTIVE: We conducted a cross-sectional study to determine if aerobic capacity and health related quality of life was decreased in HIV-infected patients receiving highly active antiretroviral therapy and comparing patients with and without lipodystrophy. RESEARCH DESIGN AND METHODS: HIV-infected patients older
than 18 years, and in current use of highly active antiretroviral therapy drugs, were evaluated for blood count, fasting total cholesterol, high density lipoprotein, triglycerides, glucose, HIV viral load and CD4/CD8 counts, body composition, peak oxygen consumption (peak VO2) and metabolic equivalent. Health related quality of life was assessed by using Short Form-36 (SF-36). Statistical analysis was carried out using SPSS version 20.0. RESULTS: A total of 63 patients with mean age of 43.1+/-6.4 years were evaluated, of these 34 (54%) had lipodystrophy. The average peak VO2 (31.4+/-7.6mLkg-1min-1) was significantly lower (p<0.01) than expected values (37.9+/-5.6mLkg-1min-1) according to the characteristics of the patients. The lipodystrophy group presented with a significant difference in muscle mass, body fat, peak VO2 and metabolic equivalent and in functional capacity domains of SF-36. CONCLUSION: Aerobic capacity values were reduced in HIV-infected patients under highly active antiretroviral therapy when compared to predicted values. Lipodystrophy was associated with reduced aerobic capacity and higher frequency of metabolic syndrome. Lifestyle modification should be a priority in the management of chronic HIV disease.


BACKGROUND: Many HIV-infected patients demonstrate disability and lower aerobic capacity. The inclusion of resistance training combined with aerobic exercise in a single program is known as combined aerobic and resistance exercise (CARE) and seems to be an effective strategy to improve muscle weakness, as well as aerobic capacity in HIV-infected patients. We performed a meta-analysis to investigate the effects of CARE in HIV-infected patients. METHODS: We searched MEDLINE, Cochrane Controlled Trials Register, EMBASE, CINAHL (from the earliest date available to August 2014) for controlled trials that evaluated the effects of CARE in HIV-infected patients. Weighted mean differences (WMD) and 95% confidence intervals (CIs) were calculated, and heterogeneity was assessed using the I2 test. RESULTS: Seven studies met the study criteria. CARE resulted in improvement in Peak VO2 WMD (4.48 mL.kg-1.min-1 95% CI: 2.95 to 6.0), muscle strength of the knee extensors WMD (25.06 Kg 95% CI: 10.46 to 39.66) and elbow flexors WMD (4.44 Kg 95% CI: 1.22 to 7.67) compared with no exercise group. The meta-analyses also showed significant improvement in Health status, Energy/Vitality and physical function domains of quality of life for participants in the CARE group compared with no exercise group. A nonsignificant improvement in social function domain of quality of life was found for participants in the CARE group compared with no exercise group. CONCLUSIONS: Combined aerobic and resistance exercise may improve peak VO2, muscle strength and health status, energy and physical function domains of quality of life and should be considered as a component of care of HIV-infected individuals.


Fatigue is common among persons living with HIV (PLWH), and risk factors for obstructive sleep apnea (OSA) such as older age and obesity are increasingly prevalent. Studies of OSA among PLWH are lacking, so we aimed to characterize OSA symptoms and associated clinical consequences (e.g., fatigue) among a contemporary population of PLWH. Self-administered surveys containing 23 items that included self-reported snoring, witnessed apneas, estimated sleep duration, the Epworth Sleepiness Score (ESS), and the FACIT-Fatigue score were mailed to PLWH receiving care at an urban HIV clinic. Clinical/demographic data were collected from the medical record. Multivariable linear regression models were created to study relationships between fatigue, clinical variables, and OSA symptoms. Of 535 surveys, 203 (38%) responded. Eight patients (3.9%) had known OSA. Among those without known OSA, mean respondent characteristics included: age 47 years; 80% male, 41% African American, 48% Caucasian, BMI 26.4 kg/m(2), duration of HIV diagnosis 12 years, 93% on antiretroviral therapy, and 81% with <50 HIV RNA copies/mL.
27% reported snoring, 24% reported witnessed apneas, and 38% had excessive daytime sleepiness. Witnessed apnea was the strongest independent predictor of fatigue (lower FACIT-Fatigue score; beta = -6.49; p < 0.001); this difference of 6.49 points exceeds the accepted minimal clinically important difference of 3.0 points. Other predictors included opioid use (beta = -5.53; p < 0.001), depression (beta = -4.18; p = 0.02), antidepressant use (beta = -4.25; p = 0.02), and sleep duration < 6 h (beta = -3.42; p = 0.02). Our data strongly support the need for increased efforts directed at OSA screening and treatment in PLWH.


BACKGROUND: Cerebrovascular disease is a cause of morbidity in HIV-infected populations. The relationship among HIV infection, brain arterial remodeling, and stroke is unclear. METHODS: Large brain arteries (n = 1,878 segments) from 284 brain donors with and without HIV were analyzed to obtain media and wall thickness and lumen-to-wall ratio, and to determine the presence of atherosclerosis and dolichoectasia (arterial remodeling extremes). Neuropathologic assessment was used to characterize brain infarcts. Multilevel models were used to assess for associations between arterial characteristics and HIV. Associations between arterial characteristics and brain infarcts were examined in HIV+ individuals only. RESULTS: Adjusting for vascular risk factors, HIV infection was associated with thicker arterial walls and smaller lumen-to-wall ratios. Cerebral atherosclerosis accounted for one-quarter of the brain infarcts in HIV+ cases, and was more common with aging, diabetes, a lower CD4 nadir, and a higher antemortem CD4 count. In contrast, a higher lumen-to-wall ratio was the only arterial predictor of unexplained infarcts in HIV+ cases. Dolichoectasia was more common in HIV+ cases with smoking and media thinning, and with protracted HIV infection and a detectable antemortem viral load. CONCLUSIONS: HIV infection may predispose to inward remodeling compared to uninfected controls. However, among HIV+ cases with protracted immunosuppression, outward remodeling is the defining arterial phenotype. Half of all brain infarcts in this sample were attributed to the extremes of brain arterial remodeling: atherosclerosis and dolichoectasia. Understanding the mechanisms influencing arterial remodeling will be important in controlling cerebrovascular disease in the HIV-infected population.

Heigele, A., et al. (2015). "Increased susceptibility of CD4+ T cells from elderly individuals to HIV-1 infection and apoptosis is associated with reduced CD4 and enhanced CXCR4 and FAS surface expression levels." Retrovirology 12: 86.

BACKGROUND: Elderly HIV-1 infected individuals progress to AIDS more frequently and rapidly than people becoming infected at a young age. To identify possible reasons for these differences in clinical progression, we performed comprehensive phenotypic analyses of CD4+ T cells from uninfected young and elderly individuals, and examined their susceptibility to HIV-1 infection and programmed death. RESULTS: Peripheral blood mononuclear cells (PBMCs) from older people contain an increased percentage of central memory and Th17 CD4+ T cells that are main target cells of HIV-1 and strongly reduced proportions of naive T cells that are poorly susceptible to HIV-1. Unstimulated T cells from elderly individuals expressed higher levels of activation markers, death receptors, and the viral CXCR4 co-receptor than those from young individuals but responded poorly to stimulation. CD4+ T cells from older individuals were highly susceptible to CXCR4- and CCR5-tropic HIV-1 infection but produced significantly lower quantities of infectious virus than cells from young individuals because they were highly prone to apoptosis and thus presumably had a very short life span. The increased susceptibility of T cells from the elderly to HIV-1 infection correlated directly with CXCR4 and inversely with CD4 expression. The levels of apoptosis correlated with the cell surface expression of FAS but not with the expression of programmed death receptor 1 (PD1) or tumor necrosis factor-related apoptosis-inducing ligand (TRAIL). CONCLUSIONS: Increased levels of activated and highly susceptible HIV-1 target cells, reduced CD4 and enhanced CXCR4 cell surface expression, together with the high susceptibility to
FAS-induced programmed cell death may contribute to the rapid CD4+ T cell depletion and accelerated clinical course of infection in elderly HIV-1-infected individuals.


**BACKGROUND:** Infection with the Human Immunodeficiency Virus-1 (HIV) is associated with clinical symptoms of accelerated aging, as evidenced by increased incidence and diversity of age-related illnesses at relatively young ages that is supported by findings of organ and cellular pathology. But it has been difficult to detect an accelerated aging effect on a molecular level. **METHODS:** Here, we applied an epigenetic biomarker of aging based on host DNA methylation levels to study accelerated aging effects due to HIV infection. DNA from brain and blood tissue was assayed via the Illumina Infinium Methylation 450K platform. **RESULTS:** Using six novel DNA methylation data sets, we show that HIV leads to an increase in epigenetic age both in brain (7.4 years) and blood (5.2 years) tissue. While the observed accelerated aging effects in blood may reflect changes in blood cell composition (notably exhausted cytotoxic T cells), it is less clear what explains the observed accelerated aging effects in brain tissue. **CONCLUSIONS:** Overall, our results demonstrate that the epigenetic clock is a useful biomarker for detecting accelerated aging effects due to HIV infection. This tool can be used to accurately determine the extent of age acceleration in individual tissue and cells.


**OBJECTIVE:** To evaluate the role of neurocognitive impairment on retention in care across the lifespan in antiretroviral-naive persons newly diagnosed with HIV. **DESIGN:** A prospective observational study of 138 antiretroviral-naive newly diagnosed HIV-positive participants who presented to an urban clinic between August 2010 and April 2013. **METHODS:** All participants underwent a baseline evaluation that included a neuromedical examination and brief neuropsychological test battery. Retention in care was operationalized as attending at least two visits separated by more than 90 days during the 12-month follow-up period. **RESULTS:** Fifty-five per cent of participants were retained in care over the study observation period. In a logistic regression controlling for ethnicity, there was a significant interaction between age and neurocognitive impairment in predicting retention in care (P = 0.009). Planned post-hoc analyses showed that neurocognitive impairment was associated with a significantly lower likelihood of retention in care among participants aged 50 years and older (P = .007), but not among younger participants (P > 0.05). **CONCLUSION:** Extending prior research on antiretroviral adherence and medication management, findings from this study indicate that neurocognitive impairment may be an especially salient risk factor for poor retention in care among older adults with newly diagnosed HIV infection.


The increased prevalence of HIV among adults >50 years underscores the importance of improving our understanding of mechanisms causing HIV-associated neurocognitive disorders (HAND). Identifying novel and noninvasive diagnostic predictors of HAND prior to clinical manifestation is critical to ultimately identifying means of preventing progression to symptomatic HAND. Here, using a task-switching paradigm, in which subjects were cued (unpredictably) to perform a face-gender or a word-semantic task on superimposed face and word images, we examined the behavioral and neural profile of impaired cognitive control in older HIV + adults (N = 14, 9 HIV+). Functional magnetic resonance imaging (fMRI) and behavioral data were acquired while subjects were performing the
face-gender or word-semantic task. We found that, despite comparable performance in standard neuropsychology tests that are designed to probe executive deficits, HIV-infected participants were significantly slower than uninfected controls in adapting to change in task demand, and the behavioral impairments can be quantitatively related to difference in fMRI signal at the dorsal anterior cingulate cortex (ACC). Due to the limited sample size of this hypothesis-generating study, we should take caution with these findings and future studies with a large and better matched sample size are needed. However, these rather novel findings in this study have a few important implications: first, the prevalence of cognitive impairments in HIV+ older adults might even be higher than previously proposed; second, ACC (in particular its dorsal region) might be one of the key regions underlying cognitive impairments (in particularly executive functions) in HIV; and third, it might be beneficial to adopt paradigms developed and validated in cognitive neuroscience to study HAND, as these techniques might be more sensitive to some aspects of HIV-associated neurocognitive impairments than standard neuropsychology tests.


Human leukocyte antigen (HLA) class I-associated polymorphisms in HIV-1 that persist upon transmission to HLA-mismatched hosts may spread in the population as the epidemic progresses. Transmission of HIV-1 sequences containing such adaptations may undermine cellular immune responses to the incoming virus in future hosts. Building upon previous work, we investigated the extent of HLA-associated polymorphism accumulation in HIV-1 polymerase (Pol) through comparative analysis of linked HIV-1/HLA class I genotypes sampled during historic (1979 to 1989; n = 338) and modern (2001 to 2011; n = 278) eras from across North America (Vancouver, BC, Canada; Boston, MA; New York, NY; and San Francisco, CA). Phylogenies inferred from historic and modern HIV-1 Pol sequences were star-like in shape, with an inferred most recent common ancestor (epidemic founder virus) sequence nearly identical to the modern North American subtype B consensus sequence. Nevertheless, modern HIV-1 Pol sequences exhibited roughly 2-fold-higher patristic (tip-to-tip) genetic distances than historic sequences, with HLA pressures likely driving ongoing diversification. Moreover, the frequencies of published HLA-associated polymorphisms in individuals lacking the selecting HLA class I allele was on average approximately 2.5-fold higher in the modern than in the historic era, supporting their spread in circulation, though some remained stable in frequency during this time. Notably, polymorphisms restricted by protective HLA alleles appear to be spreading to a greater relative extent than others, though these increases are generally of modest absolute magnitude. However, despite evidence of polymorphism spread, North American hosts generally remain at relatively low risk of acquiring an HIV-1 polymerase sequence substantially preadapted to their HLA profiles, even in the present era. IMPORTANCE: HLA class I-restricted cytotoxic T-lymphocyte (CTL) escape mutations in HIV-1 that persist upon transmission may accumulate in circulation over time, potentially undermining host antiviral immunity to the transmitted viral strain. We studied >600 experimentally collected HIV-1 polymerase sequences linked to host HLA information dating back to 1979, along with phylogenetically reconstructed HIV-1 sequences dating back to the virus' introduction into North America. Overall, our results support the gradual spread of many-though not all-HIV-1 polymerase immune escape mutations in circulation over time. This is consistent with recent observations from other global regions, though the extent of polymorphism accumulation in North America appears to be lower than in populations with high seroprevalence, older epidemics, and/or limited HLA diversity. Importantly, the risk of acquiring an HIV-1 polymerase sequence at transmission that is substantially preadapted to one's HLA profile remains relatively low in North America, even in the present era.

BACKGROUND: Immunological non-response (INR) despite virological suppression is associated with AIDS-defining events/death (ADE). Little is known about its association with serious non-AIDS-defining events (nADE).

METHODS: Patients highly-active antiretroviral therapy (HAART) with <200 CD4+/μl and achieving HIV-RNA <50 copies/ml within 12 (+/-3) months were categorized as INR if CD4+ T-cell count at year 1 was <200/μl. Predictors of nADE (malignancies, severe infections, renal failure--ie, estimated glomerular filtration rate <30 ml/min, cardiovascular events and liver decompensation) were assessed using multivariable Cox models. Follow-up was right-censored in case of HAART discontinuation or confirmed HIV-RNA>50. RESULTS: 1221 patients were observed for a median of 3 (IQR: 1.3-6.1) years. Pre-HAART CD4+ were 77/μl (IQR: 28-142) and 56% of patients had experienced an ADE. After 1 year, CD4+ increased to 286 (IQR: 197-387), but 26.1% of patients were INR. Thereafter, 86 nADE (30.2% malignancies, 27.9% infectious, 17.4% renal, 17.4% cardiovascular, 7% hepatic) were observed, accounting for an incidence of 1.83 events (95%CI: 1.73-2.61) per 100 PYFU. After adjusting for measurable confounders, INR had a significantly greater risk of nADE (HR 1.65; 95%CI: 1.06-2.56). Older age (per year, HR 1.03; 95%CI: 1.01-1.05), hepatitis C co-infection (HR 2.09; 95%CI: 1.19-3.7), a history of previous nADE (HR 2.16; 95%CI: 1.06-4.4) and the occurrence of ADE during the follow-up (HR 2.2; 95%CI: 1.15-4.21) were other independent predictors of newly diagnosed nADE.

CONCLUSIONS: Patients failing to restore CD4+ to >200 cells/μl run a greater risk of serious nADE, which is intertwined or predicted by AIDS progression. Improved management of this fragile population and innovative therapy able to induce immune-reconstitution are urgently needed. Also, our results strengthen the importance of earlier diagnosis and HAART introduction.


BACKGROUND: The risk of liver enzyme elevation (LEE) after different ritonavir-boosted protease inhibitors (PI/r) has not been fully assessed in real-life settings and in populations with high rates of hepatitis C virus (HCV) coinfection. METHODS: Patients introducing a new PI/r between 1998 and 2012 were included, if transaminases and HCV antibody (Ab) were assessed before treatment initiation. Time to grade 3 and 4 LEE were assessed during treatment initiation. RESULTS: A total of 6193 HIV-infected patients (3242 HCV-Ab negative and 2951 HCV-Ab positive) were included. Incidence of grade 3 LEE was 1.05, 7.66, and 8.08 per 100 patient-years of follow-up among HCV-Ab negative, HCV-Ab-positive and HCV-RNA-positive patients, respectively. Among HCV-Ab-negative patients, no differences were detected between different PI/r. Use of darunavir/ritonavir was not associated with LEE among HCV-coinfected patients. Atazanavir/ritonavir use was associated with grade 3 LEE but only among HCV-Ab-positive patients (versus LPV/r, hazard ratio: 1.39; 95% confidence interval: 1.1 to 1.75). This risk was not confirmed in a subanalysis restricted to HCV-RNA-positive patients (versus LPV/r, hazard ratio: 1.16; 95% confidence interval: 0.87 to 1.55). Other independent predictors of grade 3 LEE among HCV-Ab-positive patients were older age, male gender, being treatment naive, nonnucleoside reverse transcriptase inhibitor coadministration, increased aspartate aminotransferase at baseline, overweight, positive HCV-RNA, and advanced estimated liver fibrosis. CONCLUSIONS: Occurrence of hepatotoxicity was a rare finding among HCV-Ab-negative patients and was not influenced by the type of PI/r. In particular, the use of darunavir/ritonavir, previously linked with severe cases of hepatotoxicity, was not associated with a greater risk of LEE, irrespective from HCV serostatus.


HIV infection leads to age-related conditions in relatively young persons. HIV-associated neurocognitive disorders (HAND) are considered among the most prevalent of these conditions. To study the mechanisms underlying...
this disorder, researchers need an accurate method for measuring biological aging. Here, we apply a recently developed measure of biological aging, based on DNA methylation, to the study of biological aging in HIV+ brains. Retrospective analysis of tissue bank specimens and pre-mortem data was carried out. Fifty-eight HIV+ adults underwent a medical and neurocognitive evaluation within 1 year of death. DNA was obtained from occipital cortex and analyzed with the Illumina Infinium Human Methylation 450K platform. Biological age determined via the epigenetic clock was contrasted with chronological age to obtain a measure of age acceleration, which was then compared between those with HAND and neurocognitively normal individuals. The HAND and neurocognitively normal groups did not differ with regard to demographic, histologic, neuropathologic, or virologic variables. HAND was associated with accelerated aging relative to neurocognitively normal individuals, with average relative acceleration of 3.5 years. Age acceleration did not correlate with pre-mortem neurocognitive functioning or HAND severity. This is the first study to demonstrate that the epigenetic age of occipital cortex samples is associated with HAND status in HIV+ individuals pre-mortem. While these results suggest that the increased risk of a neurocognitive disorder due to HIV might be mediated by an epigenetic aging mechanism, future studies will be needed to validate the findings and dissect causal relationships and downstream effects.


The widespread use of combination antiretroviral therapy (cART) has dramatically decreased AIDS-associated morbidity and mortality in HIV-infected individuals 1. However, HIV treatment-experienced patients have a high prevalence of aging-associated diseases such as malignancies and cardiovascular diseases 2. Given the canonical role of the telomerase system in cellular aging, it has been implicated in the pathogenesis of these non-AIDS defining illnesses in HIV-infected individuals 3. This article is protected by copyright. All rights reserved.


Bacterial and viral infections of the gastrointestinal tract are more common in the elderly and represent a major cause of morbidity and mortality. The mucosal immune system provides the first line of defence against pathogens acquired by ingestion and inhalation, but its function is adversely affected in the elderly. This aging-related decline in the immune function is termed immunosenescence and is associated with diminished abilities to generate protective immunity, reduced vaccine efficacy, increased incidence of cancer, inflammation and autoimmunity, and the impaired ability to generate tolerance to harmless antigens. In this review we describe our current understanding of the effects immunosenescence has on the innate and adaptive arms of the mucosal immune system in the intestine. Current estimates suggest that by the year 2050 up to 40% of the UK population will be over 65 years old, bringing with it important health challenges. A thorough understanding of the mechanisms that contribute to the development of immunosenescence is therefore crucial to help identify novel approaches to improve mucosal immunity in the elderly.


T-cell defects, immune suppression, and poor antitumor immune responses are hallmarks of chronic lymphocytic leukemia (CLL), and PD-1/PD-L1 inhibitory signaling has emerged as a major immunosuppressive mechanism. However, the effect of different microenvironments and the confounding influence of aging are poorly
understood. The current study uses the Emu-TCL1 mouse model, which replicates human T-cell defects, as a preclinical platform to longitudinally examine patterns of T-cell dysfunction alongside developing CLL and in different microenvironments, with a focus on PD-1/PD-L1 interactions. The development of CLL was significantly associated with changes in T-cell phenotype across all organs and function. Although partly mirrored in aging wild-type mice, CLL-specific T-cell changes were identified. Murine CLL cells highly expressed PD-L1 and PD-L2 in all organs, with high PD-L1 expression in the spleen. CD3(+)CD8(+) T cells from leukemic and aging healthy mice highly expressed PD-1, identifying aging as a confounder, but adoptive transfer experiments demonstrated CLL-specific PD-1 induction. Direct comparisons of PD-1 expression and function between aging CLL mice and controls identified PD-1(+) T cells in CLL as a heterogeneous population with variable effector function. This is highly relevant for therapeutic targeting of CD8(+) T cells, showing the potential of reprogramming and selective subset expansion to restore antitumor immunity.


Older HIV-infected adults have a higher risk of neurocognitive impairment, but the underlying mechanisms are poorly understood. Here, we investigated the associations between levels of HIV DNA in peripheral blood, soluble markers of inflammation and cellular trafficking in blood and cerebrospinal fluid (CSF) and neurocognitive functioning among 18 younger (22-40 years) and 26 older (50-71 years) HIV-infected subjects, who were administered a comprehensive neurocognitive battery. Older HIV-infected individuals presented higher levels of inflammation in CSF and blood compared to younger individuals, but no difference was observed in HIV DNA levels. Among older participants, higher HIV DNA levels were significantly associated with more severe neurocognitive impairment (p = 0.005), particularly in the Executive Functions domain (p = 0.004). No association was observed between HIV DNA and neurocognition among younger individuals. Despite significantly increased inflammation observed in the older group, none of the inflammatory markers were associated with neurocognitive impairment among older HIV+ individuals (p > 0.05). Our study supports the involvement of peripheral HIV DNA reservoir in the pathogenesis of neurocognitive disorder during suppressive ART. Correlates of neurocognitive impairment might differ between younger and older adults, suggesting that future treatment and prevention strategies for HIV-associated neurocognitive disorders likely need to be tailored based on age.


Older individuals often experience declines in cognitive function after events (e.g. infection, or injury) that trigger activation of the immune system. This occurs at least in part because aging sensitizes the response of microglia (the brain's resident immune cells) to signals triggered by an immune challenge. In the aging brain, microglia respond to these signals by producing more pro-inflammatory cytokines (e.g. interleukin-1beta or IL-1beta) and producing them for longer than microglia in younger brains. This exaggerated inflammatory response can compromise processes critical for optimal cognitive functioning. Interleukin-1beta is central to the inflammatory response and is a key mediator and modulator of an array of associated biological functions; thus its production and release is usually very tightly regulated. This review will focus on the impact of dysregulated production of IL-1beta on hippocampus dependent-memory systems and associated synaptic plasticity processes. The neurotrophin brain-derived neurotrophic factor (BDNF) helps to protect neurons from damage caused by infection or injury, and it plays a critical role in many of the same memory and hippocampal plasticity processes compromised by dysregulated production of IL-1beta. This suggests that an exaggerated brain inflammatory response, arising from aging and a secondary immune challenge, may erode the capacity to provide the BDNF needed for memory-related plasticity processes at hippocampal synapses. This article is part of a Special Issue entitled 'Neuroimmunology and Synaptic Function'.

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Patients with treated HIV-1 infection experience earlier occurrence of aging-associated diseases, raising speculation that HIV-1 infection, or antiretroviral treatment, may accelerate aging. We recently described an age-related co-methylation module comprised of hundreds of CpGs; however, it is unknown whether aging and HIV-1 infection exert negative health effects through similar, or disparate, mechanisms. We investigated whether HIV-1 infection would induce age-associated methylation changes. We evaluated DNA methylation levels at >450,000 CpG sites in peripheral blood mononuclear cells (PBMC) of young (20-35) and older (36-56) adults in two separate groups of participants. Each age group for each data set consisted of 12 HIV-1-infected and 12 age-matched HIV-1-uninfected samples for a total of 96 samples. The effects of age and HIV-1 infection on methylation at each CpG revealed a strong correlation of 0.49, p<1 x 10^-200 and 0.47, p<1 x 10^-200. Weighted gene correlation network analysis (WGCNA) identified 17 co-methylation modules; module 3 (ME3) was significantly correlated with age (cor=0.70) and HIV-1 status (cor=0.31). Older HIV-1+ individuals had a greater number of hypermethylated CpGs across ME3 (p=0.015). In a multivariate model, ME3 was significantly associated with age and HIV status (Data set 1: betaage=0.007088, p=2.08 x 10^-9; betahIV=0.099574, p=0.0011; Data set 2: betaage=0.008762, p=1.27 x 10^-5; betahIV=0.128649, p=0.0001). Using this model, we estimate that HIV-1 infection accelerates age-related methylation by approximately 13.7 years in data set 1 and 14.7 years in data set 2. The genes related to CpGs in ME3 are enriched for polycomb group target genes known to be involved in cell renewal and aging. The overlap between ME3 and an aging methylation module found in solid tissues is also highly significant (Fisher-exact p=5.6 x 10^-6, odds ratio=1.91). These data demonstrate that HIV-1 infection is associated with methylation patterns that are similar to age-associated patterns and suggest that general aging and HIV-1 related aging work through some common cellular and molecular mechanisms. These results are an important first step for finding potential therapeutic targets and novel clinical approaches to mitigate the detrimental effects of both HIV-1 infection and aging.
resonance imaging (MRI), and more recently with diffusion tensor imaging (DTI). This study investigates the combined effects of age and HIV serostatus on WMH and DTI measures, as well as the relationships between these white matter measures, in 88 HIV seropositive (HIV+) and 49 seronegative (HIV-) individuals aged 23-79 years. A whole-brain volumetric measure of WMH was quantified from FLAIR images using a semi-automated process, while fractional anisotropy (FA) was calculated for 15 regions of a whole-brain white matter skeleton generated using tract-based spatial statistics (TBSS). An age by HIV interaction was found indicating a significant association between WMH and older age in HIV+ participants only. Similarly, significant age by HIV interactions were found indicating stronger associations between older age and decreased FA in the posterior limbs of the internal capsules, cerebral peduncles, and anterior corona radiata in HIV+ vs. HIV- participants. The interactive effects of HIV and age were stronger with respect to whole-brain WMH than for any of the FA measures. Among HIV+ participants, greater WMH and lower anterior corona radiata FA were associated with active hepatitis C virus infection, a history of AIDS, and higher current CD4 cell count. Results indicate that age exacerbates HIV-associated abnormalities of whole-brain WMH and fronto-subcortical white matter integrity.


BACKGROUND: There is a significant increase in the number of HIV-infected older adults (HOA). This population may experience functional decline at a much younger age. Little is known about the relationship between functional limitations and systemic adipokines in HOA. OBJECTIVE: Our study aimed to evaluate the relationship between functional limitations and systemic adipokine levels in HOA population. DESIGN: Cross-sectional. SETTING: Academic hospital-based infectious disease clinic. PARTICIPANTS: The study investigated community-dwelling HIV-infected adults >50 years old and compared this group with age, gender and BMI comparable healthy controls. MEASUREMENTS: We measured functional status, body composition and plasma concentrations of adipokines. RESULTS: Fifty-four HOA were studied (mean: age 57 years, BMI 29 kg/m2, CD4 604, duration of HIV 17 years) and compared with thirty-two age, gender and BMI comparable healthy controls. The HOA group showed significantly higher functional limitations compared to the age, gender and BMI comparable controls (p<0.05). Levels of adipokines were significantly different between the two groups (p<0.05). Multiple regression analyses indicated that adiponectin and visfatin were significantly correlated with several physical function measures after controlling for age, sex, and metabolic comorbidities. Adiponectin was negatively correlated with functional limitations, and this relationship was stronger in the control group compared to the HOA group. Conversely, visfatin was positively correlated with functional limitations only in the HOA group. CONCLUSION: HOA have significant functional limitations and alteration in adipokine levels compared to controls. Adiponectin and visfatin were associated with functional limitations. Visfatin was a correlate of physical function only in the HOA group. Prospective longitudinal studies could provide further insight on the role of adipokines in HIV-related functional decline.


With the rising number of individuals in their 50s and 60s who are infected with HIV, concerns have emerged about possible increases in the rates of non-HIV-associated dementias. The current study examined the prevalence of mild cognitive impairment (MCI) in older HIV-infected adults, since MCI is an intermediate state between typical cognitive aging and dementia that emerges in this age range. Participants included 75 adults with HIV disease aged 50 years and older who were on combination antiretroviral therapy (cART) and had undetectable plasma viral loads and 80 demographically similar HIV-seronegative comparison subjects. Participants completed a research neuropsychological evaluation that was used to classify MCI according to the comprehensive diagnostic scheme.
described by Bondi et al. (J Alzheimers Dis 42:275-289, 2014). HIV-infected persons were over seven times more likely to have an MCI designation (16 %) than their seronegative counterparts (2.5 %). Within the HIV+ cohort, MCI had minimal overlap with diagnoses of asymptomatic neurocognitive impairment and was significantly associated with older age, lower Karnofsky Scale of Performance Scores, and mild difficulties performing instrumental activities of daily living (iADLs). HIV infection in older adults is associated with a notably elevated concurrent risk of MCI, which may increase the likelihood of developing non-HIV-associated dementias as this population ages further.


HIV infection is associated with arterial stiffness, but no studies have assessed this relationship in sub-Saharan Africa. We enrolled 205 participants over 40 years old in Uganda: 105 on antiretroviral therapy for a median of 7 years, and a random sample of 100 age and sex-matched HIV-uninfected controls from the clinic catchment area. The prevalence of arterial stiffness (ankle brachial index > 1.2) was 33%, 18%, 19% and 2% in HIV+ men, HIV- men, HIV+ women, and HIV- women. In multivariable models adjusted for cardiovascular risk factors, HIV+ individuals had over double the prevalence of arterial stiffness (adjusted prevalence ratio 2.86, 95% confidence interval 1.41-5.79, P = 0.003).


Over the past three decades, perinatal HIV infection in the United States has evolved from a fatal disease to a manageable chronic illness. As the majority of youth with perinatal HIV infection age into adolescence and adulthood, management of this stigmatizing, transmittable disease in the backdrop of a cadre of environmental stressors presents challenges beyond those of other chronic illnesses. The neurologic and neuropsychological consequences of this neurotropic virus have important implications for the successful navigation of responsibilities related to increasingly independent living of this aging population. This article will review the neurologic and neuropsychological consequences of perinatal HIV infection and concomitant factors in the era of highly active antiretroviral therapy and will provide an overview of the neuropathology, pathogenesis, neuroimaging findings, and treatment of perinatal HIV infection, as well as recommendations for service provision and future research.


Graph theory models can produce simple, biologically informative metrics of the topology of resting-state functional connectivity (FC) networks. However, typical graph theory approaches model FC relationships between regions (nodes) as unweighted edges, complicating their interpretability in studies of disease or aging. We extended existing techniques and constructed fully connected weighted graphs for groups of age-matched human immunodeficiency virus (HIV) positive (n = 67) and HIV negative (n = 77) individuals. We compared test-retest reliability of weighted versus unweighted metrics in an independent study of healthy individuals (n = 22) and found weighted measures to be more stable. We quantified 2 measures of node centrality (closeness centrality and eigenvector centrality) to capture the relative importance of individual nodes. We also quantified 1 measure of graph entropy (diversity) to measure the variability in connection strength (edge weights) at each node. HIV was primarily associated with differences in measures of centrality, and age was primarily associated with differences in diversity. HIV and age were associated with divergent measures when evaluated at the whole graph level, within individual
functional networks, and at the level of individual nodes. Graph models may allow us to distinguish previously indistinguishable effects related to HIV and age on FC.


BACKGROUND: We examined trends in adherence to highly active antiretroviral therapy (HAART) and HIV RNA suppression and estimated the minimum cutoff of adherence to newer HAART formulations needed for HIV RNA suppression by regimen type. METHODS: We used Veterans Affairs pharmacy dispensing data from the Veterans Aging Cohort Study Virtual Cohort between October 2000 and September 2010 and defined adherence as the duration of time the patient had the medications available, relative to the total number of days between refills for all antiretrovirals in a year. Temporal trends in adherence and viral load suppression were examined by the patient's most frequently used HAART regimen in the year. The minimum needed adherence was defined as the level at which the odds of suppression was not significantly different than that observed with >/= 95% adherence using repeated-measures logistic regression. RESULTS: A total of 21,865 HAART users contributed 82,217 person-years of follow-up. There was a significant increase (P(trend) < 0.001) in the proportion virally suppressed even among those with <95% adherence (2001: 38% to 2010: 84%), and the trend was similar when restricting to their first HAART regimen. For nonnucleoside reverse transcriptase inhibitor multi-pill users, the odds of suppression did not differ for 85%-89% adherence compared to those with >/= 95% adherence [odds ratios: 0.82 (0.64-1.04)], but for protease inhibitor users, the odds of suppression significantly differed if adherence levels were <95% compared to >/= 95% adherence. CONCLUSIONS: Although all HIV-infected persons should be instructed to achieve perfect adherence, concerns of slightly lower adherence should not hinder prescribing new HAART regimens early in HIV infection.


Over 50% of HIV+ individuals exhibit neurocognitive impairment and subcortical atrophy, but the pattern of brain abnormalities associated with HIV is still poorly understood. Using parametric surface-based shape analyses, we mapped the 3D profile of subcortical morphometry in 63 HIV+ participants and 31 uninfected controls. The thalamus, corpus striatum, hippocampus, amygdala, brainstem, callosum and ventricles were segmented from brain MRIs. To investigate subcortical shape, we analyzed the Jacobian determinant (JD) and radial distances (RD) for structure surfaces. We also investigated effects of nadir CD4+ T-cell counts, viral load, and illness duration on subcortical morphology. Our results characterize subcortical morphometry in older HIV+ people, where participants showed significant volumetric enlargements in the thalamus, left pallidum and the ventricles while showing a reduction in the callosum. Further, RD maps revealed atrophy of the left thalamus and expansion of the brainstem in HIV. RD and JD maps of the right pallidum identified tissue expansion associated with illness duration while the left pallidum showed anterior atrophy and posterior expansion associated with viral load.


BACKGROUND: Systemic immune activation (inflammation) and immunosenescence develop in some people with advancing age. This process, known as "inflam-aging," is associated with physical frailty and sarcopenia. Meanwhile, successful antiretroviral therapy has led to a growing number of older HIV-1-infected individuals who face both age-related and HIV-1-related inflammation, which may synergistically promote physical decline, including
frailty and sarcopenia. The purpose of our study was to determine if inflammation during treated HIV-1 infection worsens physical impairment in older individuals. METHODS: We determined the severity of HIV-associated inflammation and physical performance (strength and endurance) in 21 older HIV-infected individuals (54-69 years) receiving suppressive antiretroviral therapy, balanced for confounding variables including age, anthropometrics, and co-morbidities with 10 uninfected control individuals. Biomarkers for microbial translocation (lipopolysaccharide [LPS]), inflammation (soluble CD14 [sCD14], osteopontin, C-reactive protein [CRP], interleukin-6 [IL-6], soluble ICAM-1 [sICAM-1] and soluble VCAM-1 [sVCAM-1]), and coagulopathy (D-dimer) were assayed in plasma. Activation phenotypes of CD4(+)T cells, CD8(+) T cells and monocytes were measured by flow cytometry. Physical performance was measured by 400 m walking speed, a short physical performance battery [SPPB], and lower extremity muscle strength and fatigue. RESULTS: Overall physical function was similar in the uninfected and HIV-infected groups. Compared to uninfected individuals, the HIV-infected group had elevated levels of sCD14 (P < 0.001), CRP (P < 0.001) and IL-6 (P = 0.003) and an increased frequency of CD4(+) and CD8(+) T cells with an immunosenescent CD57(+) phenotype (P = 0.004 and P = 0.043, respectively). Neither plasma inflammatory biomarkers nor CD57(+) T cells correlated with CD4(+) T cell counts. Furthermore, none of the elevated inflammatory biomarkers in the HIV-infected subjects were associated with any of the physical performance results. CONCLUSIONS: When age-related co-morbidities were carefully balanced between the uninfected and HIV-infected groups, no evidence of inflammation-associated physical impairment was detected. Despite careful balancing for age, BMI, medications and co-morbidities, the HIV-infected group still displayed evidence of significant chronic inflammation, including elevated sCD14, CRP, IL-6 and CD57(+) T cells, although the magnitude of this inflammation was unrelated to physical impairment.


OBJECTIVE: To investigate the relationship between cognitive impairment and hippocampal morphological and functional changes in HIV-seropositive patients. METHODS: Thirty HIV+ patients who complain of memory decrease and 15 healthy volunteers were recruited. Performances of learning and memory were assessed using Hopkins Verbal Learning Test-Revised (HVLT-R) and Brief Visuospatial Memory Test-Revised (BVMT-R). Bilateral hippocampal volume, apparent diffusion coefficient (ADC) value, fractional anisotropy value, and magnetic resonance spectroscopy variables of bilateral hippocampus and parahippocampal gyrus were detected by 3.0 T magnetic resonance scanner. RESULTS: We found significant differences in all cognitive outcomes but one between HIV+ and HIV- patients. There was a difference in the ADC value of left parahippocampal gyrus between mild-impairment group and severe-impairment group (P = 0.018). We found differences in the choline (Cho), Cho/creatinine (Cr), and N-acetylaspartate/Cr of left hippocampus (P = 0.002, P = 0.008, P = 0.002) and the Cho/Cr of right parahippocampal gyrus (P = 0.023) between HIV+ and HIV- patients and in the myoinositol of left hippocampus (P = 0.003) and the glutamate and glutamine of right hippocampus (P < 0.001) between mild-impairment group and severe-impairment group. We found significant positive correlations between N-acetylaspartate/Cr of left hippocampus and outcomes of HVLT-R and BVMT-R. There were significant negative correlations between ADC values of hippocampus and parahippocampal gyrus and outcomes of HVLT-R and BVMT-R and between Cho and Cho/Cr of hippocampus and parahippocampal gyrus and outcomes of HVLT-R and BVMT-R. CONCLUSIONS: The performance of verbal learning and visual memory was significantly decreased in HIV-1-seropositive patients. The cognitive impairment of HIV infection was associated with conductive function and metabolic changes of hippocampus and parahippocampal gyrus in this study.

The relationship between markers of monocyte/macrophage activation (sCD14 and sCD163) and components of the Veterans Aging Cohort Study (VACS) score, which predict mortality in patients with HIV, in immunologic nonresponders (INRs) is not defined. HIV+ subjects with >12 months of continuous virologic suppression and persistent CD4 <250 cells/mm^3 were enrolled at the CORE Center, Chicago. Subjects had a single visit where history was taken and blood drawn. ELISA assays for sCD14 and sCD163 were performed at Blood Systems, CA. Descriptive statistics were performed using SAS. We enrolled 43 subjects with persistent CD4 <250 after a median of 32 months of continuous viral suppression. We found elevated markers of monocyte/macrophage activation; sCD14 and sCD163 correlated with higher VACS scores as well as hepatitis C virus (HCV) coinfection and FIB-4 score, components of the VACS index. In this cohort of immunologic nonresponders, there was a significant correlation between markers of monocyte/macrophage activation and the VACS score. Among components of the VACS index, we did not find a significant association between HCV coinfection and sCD14; however, there was a significant association between HCV coinfection and sCD163.


Aging confers increased susceptibility to common pathogens including influenza A virus. Despite shared vulnerability to infection with advancing age in humans and rodents, the relatively long time required for immune senescence to take hold practically restricts the use of naturally aged mice to investigate aging-induced immunological shifts. Here, we show accelerated aging Lmna(Dhe) mice with spontaneous mutation in the nuclear scaffolding protein, lamin A, replicate infection susceptibility, and substantial immune cell shifts that occur with advancing age. Naturally aged (>/>20 month) and 2- to 3-month-old Lmna(Dhe) mice share near identically increased influenza A susceptibility compared with age-matched Lmna(WT) control mice. Increased mortality and higher viral burden after influenza infection in Lmna(Dhe) mice parallel reduced accumulation of lung alveolar macrophage cells, systemic expansion of immune suppressive Foxp3(+) regulatory T cells, and skewed immune dominance among viral-specific CD8(+) T cells similar to the immunological phenotype of naturally aged mice. Thus, aging-induced infection susceptibility and immune senescence are replicated in accelerated aging Lmna(Dhe) mice.


BACKGROUND: Both HIV infection and frailty have been associated with chronic immune activation. One possible explanation for this chronic immune activation could be low levels of CD4(+) T regulatory cells (Tregs), which suppress immune responses. METHODS: HIV-uninfected (HIV-) and HIV-infected (HIV+) men in the Multicenter AIDS Cohort Study (MACS) were classified as frail (or nonfrail) if they expressed (or did not express) the Fried frailty phenotype at two consecutive study visits. Percentages and absolute numbers of total Tregs, and percentages of different subsets of Tregs and of activated T cells were measured by flow cytometry. The function of Tregs was measured by suppression of T-cell proliferation. RESULTS: Percentages of Tregs were higher, rather than lower, in frail men than in nonfrail men, and this difference was significant for HIV- men. Percentages of subsets of Tregs did not differ significantly by frailty status. Among HIV+ men, the suppressive function of Tregs was similar between frail and nonfrail men. Percentages of Tregs and activated T cells were negatively correlated in nonfrail men (HIV- and HIV+) and in frail HIV- men, but this correlation was strongly positive in frail HIV+ men. CONCLUSION: These data suggest that: (a) Tregs were not deficient in frail men; and (b) the immunological pathophysiology of frailty may differ by HIV status.
Biomarkers


OBJECTIVES: HIV-associated brain injury persists despite combination antiretroviral therapy, but contributing factors remain poorly understood. We postulated that inflammation-associated biomarkers will be associated with cerebral injury on proton magnetic resonance spectroscopy in chronically HIV-infected subjects. METHODS: Five biomarkers were measured in 197 HIV-infected subjects: soluble CD14, MCP-1, IP-10, MIP-1beta, and fractalkine. Levels of N-acetyl aspartate (NAA), Choline (Cho), Myoinositol (MI), Glutamate + Glutamine (Glx), and Creatine (Cr) were acquired in the midfrontal cortex (MFC), frontal white matter, and basal ganglia (BG). Predictive models were built through linear regression, and the best models were chosen using the Akaike Information Criterion. RESULTS: Increases in plasma or CSF MCP-1 were associated with lower NAA/Cr in the MFC and BG, whereas metabolite changes in the frontal white matter for NAA/Cr, Glx/Cr, and Cho/Cr were explained almost exclusively by a single factor, sCD14. Plasma and CSF levels of this factor were also significantly associated with Glx/Cr in MFC and BG. Higher CSF FKN was associated with higher NAA/Cr in BG. Best predictors for higher Cho/Cr in BG and MFC were CSF sCD14 and CSF MIP-1beta. Plasma and CSF IP-10 were only associated with Cho/Cr in MFC. Of the 3 models that simultaneously accounted for both plasma and CSF, there were more associations between CSF biomarkers and magnetic resonance spectroscopy metabolites. CONCLUSIONS: Markers of inflammation and immune activation, in particular MCP-1 and sCD14, predominantly reflecting CNS sources, contribute to the persistence of brain injury in a metabolite and region-dependent manner in chronically HIV-infected patients on stable combination antiretroviral therapy.


BACKGROUND: Depression is a frequent comorbidity in HIV infection that has been associated with worse treatment outcomes and increased mortality. Recent studies suggest that increased innate immune activation and tryptophan catabolism are associated with higher risk of depression in HIV infection and other chronic inflammatory diseases, but the mechanisms leading to depression remain poorly understood. METHODS: The severity of depressive symptoms was assessed by Beck Depression Inventory or Center for Epidemiological Studies Depression Scale. Untargeted metabolomic profiling of plasma from 104 subjects (68 HIV-positive and 36 HIV-negative) across 3 independent cohorts was performed using liquid or gas chromatography followed by mass spectrometry. Cytokine profiling was by Bioplex array. Bioinformatic analysis was performed in Metaboanalyst and R. RESULTS: Decreased monoamine metabolites (phenylacetate, 4-hydroxyphenylacetate) and acylcarnitines (propionylcarnitine, isobutyrylcarnitine, isovalerylcaritnine, 2-methylbutyrylcarnitine) in plasma distinguished depressed subjects from controls in HIV-positive and HIV-negative cohorts, and these alterations correlated with the severity of depressive symptoms. In HIV-positive subjects, acylcarnitines and other markers of mitochondrial function correlated inversely with tryptophan catabolism, a marker of interferon responses, suggesting interrelationships between inflammatory pathways, tryptophan catabolism, and metabolic alterations associated with depression. Altered metabolites mapped to pathways involved in monoamine metabolism, mitochondrial function, and inflammation, suggesting a model in which complex relationships between monoamine metabolism and mitochondrial bioenergetics contribute to biological mechanisms involved in depression that may be augmented by inflammation during HIV infection.
CONCLUSIONS: Integrated approaches targeting inflammation, monoamine metabolism, and mitochondrial pathways may be important for prevention and treatment of depression in people with and without HIV.


OBJECTIVES: We studied the link between T-cell activation, differentiation and senescence phenotypes and non-AIDS-related comorbidities in HIV-suppressed patients. DESIGN: Patients included in the ANRS CO3 Aquitaine Cohort were consecutively enrolled in this cross-sectional study between October 2011 and May 2013 called Chronic Immune Activation and Senescence (CIADIS) study. METHODS: We summarized immune markers [CD4 and CD8 activation (DR), differentiation (naive and terminally differentiated memory T cells), and senescence (CD57CD28)] in a weighted immune score by principal component analysis called CIADIS. Previously described Veterans Aging Cohort Study (VACS) index and immune risk profile (IRP) scores were calculated. We used adjusted logistic regression to assess the association between the CIADIS score and the presence of at least three non-AIDS-defining comorbidities.

RESULTS: Of 876 patients with an undetectable viral load, 73.4% were men and median age was 50.5 years [interquartile range (IQR) 44.7-56.7 years]. Median CD4 T-cell count was 579/mul (IQR 429-759 cells/mul), and median duration of HIV viral suppression was 5.3 years (IQR 2.3-8.7). The weighted CIADIS score was associated with at least three comorbidities (odds ratio 1.3 for 1 SD more, 95% confidence interval 1.0, 1.6) independently of age, sex, AIDS stage, and the Veterans Aging Cohort Study score. The CIADIS and the immune risk profile scores were significantly associated with at least three comorbidities in adjusted models restricted to patients younger than 60 years. None of the tested scores were associated with at least three comorbidities in patients older than 60 years. CONCLUSIONS: The weighted CIADIS score based on activation, senescence, and differentiation markers might help physicians identifying patients at a higher risk for non-AIDS-related comorbidities.


HIV-infected individuals suffer from accelerated immunologic aging. One of the most prominent changes during T lymphocyte aging is the accumulation of CD28(null) T lymphocytes, mainly CD8(+) but also CD4(+) T lymphocytes. Enhancing the functional properties of these cells may be important because they provide antigen-specific defense against chronic infections. The objective of this study was to compare the responses of CD4(+)CD28(null) and CD8(+)CD28(null) T lymphocytes from HIV-infected patients to the immunomodulatory effects of cytokines IL-15 and IL-21. We quantified the frequencies of CD4(+)CD28(null) and CD8(+)CD28(null) T lymphocytes in peripheral blood from 110 consecutive, HIV-infected patients and 25 healthy controls. Patients showed increased frequencies of CD4(+)CD28(null) and CD8(+)CD28(null). Both subsets were positively correlated to each other and showed an inverse correlation with the absolute counts of CD4(+) T lymphocytes. Higher frequencies of HIV-specific and CMV-specific cells were found in CD28(null) than in CD28(+) T lymphocytes. Activation of STAT5 by IL-15 and STAT3 by IL-21 was higher in CD28(null) compared with CD28(+) T lymphocytes. Proliferation, expression of CD69, and IFN-gamma production in CD28(null) T lymphocytes were increased after treatment with IL-15, and IL-21 potentiated most of those effects. Nevertheless, IL-21 alone reduced IFN-gamma production in response to anti-CD3 stimulation but increased CD28 expression, even counteracting the inhibitory effect of IL-15. Intracytoplasmic stores of granzyme B and perforin were increased by IL-15, whereas IL-21 and simultaneous treatment with the 2 cytokines also significantly enhanced degranulation in CD4(+)CD28(null) and CD8(+)CD28(null) T lymphocytes. IL-15 and IL-21 could have a role in enhancing the effector response of CD28(null) T lymphocytes against their specific chronic antigens in HIV-infected patients.
Human cytomegalovirus (CMV), the prototypical beta-herpervirus, is a widespread pathogen that establishes a lifelong latent infection in myeloid progenitor, and possibly other cells as well. Although immunocompetent individuals show mild or no symptoms despite periodic reactivation during myeloid cell differentiation, CMV is responsible for considerable morbidity and mortality in older adults and in persons chronically infected with HIV. Indeed, in these individuals, reactivation of CMV can cause serious complications. This review will focus on the effects of CMV during aging and HIV/AIDS, with particular attention to the cellular immunity and age-related pathology outcomes from this persistent infection. The impact of the long-term chronic exposure to CMV antigens on the expansion of CD8 T cells with features of replicative senescence will be highlighted.

Hand-grip strength is strongly correlated with measures of muscle mass and can be taken to predict morbidity and mortality. The aim of this study was to investigate the relationship between hand-grip strength and other markers associated with immune ageing, such as Cytomegalovirus (CMV) infection, leukocyte telomere length and serum levels of inflammatory and anti-inflammatory markers in the elderly. We have assessed grip strength with the Smedley Dynamometer in younger (22-37 years) and older (60-85 years) men and women in a sample of people living in Berlin (the BASE-II study). Serum cytokine levels were determined by flow-cytometry, CMV serostatus via ELISA and leukocyte telomere length by quantitative PCR. IL-1beta levels tended to be negatively associated with grip strength, but we did not find a significant association with IL-6 levels. CMV-seropositivity was not associated with higher levels of IL-1beta, IL-6 or TNF, nor with weaker grip strength in men or women at any age. A putative general measure of organismal ageing, overall leukocyte telomere length, was also found not to be associated with lower grip strength in the elderly. Hand-grip strength remains an important biomarker independent of CMV infection or shorter telomere lengths, and poorly reflected in peripheral pro-inflammatory cytokine levels, all of which have been associated in some studies with frailty and mortality.
physical capability and cognitive, physiological and musculoskeletal, endocrine and immune functions. Where available, we used existing systematic reviews, meta-analyses and other authoritative reports such as the recently launched NIH Toolbox for assessment of neurological and behavioural function, which includes test batteries for cognitive and motor function (the latter described here as physical capability). We invited international experts to comment on our draft recommendations. In addition, we hosted an experts workshop in Newcastle, UK, on 22-23 October 2012, aiming to help capture the state-of-the-art in this complex area and to provide an opportunity for the wider ageing research community to critique the proposed panel of biomarkers. DISCUSSION: Here we have identified important biomarkers of healthy ageing classified as subdomains of the main areas proposed. Cardiovascular and lung function, glucose metabolism and musculoskeletal function are key subdomains of physiological function. Strength, locomotion, balance and dexterity are key physical capability subdomains. Memory, processing speed and executive function emerged as key subdomains of cognitive function. Markers of the HPA-axis, sex hormones and growth hormones were important biomarkers of endocrine function. Finally, inflammatory factors were identified as important biomarkers of immune function. We present recommendations for a panel of biomarkers that address these major areas of function which decline during ageing. This biomarker panel may have utility in epidemiological studies of human ageing, in health surveys of older people and as outcomes in intervention studies that aim to promote healthy ageing. Further, the inclusion of the same common panel of measures of healthy ageing in diverse study designs and populations may enhance the value of those studies by allowing the harmonisation of surrogate endpoints or outcome measures, thus facilitating less equivocal comparisons between studies and the pooling of data across studies.


Combination antiretroviral therapy (cART) has extended the longevity of human immunodeficiency virus (HIV)-infected individuals. However, this has resulted in greater awareness of age-associated diseases such as chronic obstructive pulmonary disease (COPD). Accelerated cellular senescence may be responsible, but its magnitude as measured by leukocyte telomere length is unknown and its relationship to HIV-associated COPD has not yet been established. We measured absolute telomere length (aTL) in peripheral leukocytes from 231 HIV-infected adults. Comparisons were made to 691 HIV-uninfected individuals from a population-based sample. Subject quartiles of aTL were assessed for relationships with measures of HIV disease severity, airflow obstruction, and emphysema severity on computed tomographic (CT) imaging. Multivariable regression models identified factors associated with shortened aTL. Compared to HIV-uninfected subjects, the mean aTL in HIV-infected patients was markedly shorter by 27 kbp/genome (p<0.001); however, the slopes of aTL vs. age were not different (p=0.469). Patients with longer known durations of HIV infection (p=0.019) and lower nadir CD4 cell counts (p=0.023) had shorter aTL. Shorter aTL were also associated with older age (p=0.026), smoking (p=0.005), reduced forced expiratory volume in one second (p=0.030), and worse CT emphysema severity score (p=0.049). HIV-infected subjects demonstrate advanced cellular aging, yet in a cART-treated cohort, the relationship between aTL and age appears no different from that of HIV-uninfected subjects.


CD4(+)CD28(-) T cells are a unique type of proinflammatory T cells characterised by blockade of costimulatory CD28 receptor expression at the transcriptional level, which is still reversible by IL-12. In healthy individuals older than 65 years, these cells may accumulate to up to 50% of total CD4(+) T lymphocytes as in many immune-mediated diseases, immunodeficiency, and specific infectious diseases. Here we focus on CD4(+)CD28(-) T cells in chronic
immune-mediated diseases, summarizing various phenotypic and functional characteristics, which vary depending on the underlying disease, disease activity, and concurrent treatment. CD4(+)CD28(-) T cells present as effector/memory cells with increased replicative history and oligoclonality but reduced apoptosis. As an alternative costimulatory signal instead of CD28, not only natural killer cell receptors and Toll-like receptors, but also CD47, CTLA-4, OX40, and 4-1BB have to be considered. The proinflammatory and cytotoxic capacities of these cells indicate an involvement in progression and maintenance of chronic immune-mediated disease. So far it has been shown that treatment with TNF-alpha blockers, abatacept, statins, and polyclonal antilymphocyte globulins (ATG) mediates reduction of the CD4(+)CD28(-) T cell level. The clinical relevance of targeting CD4(+)CD28(-) T cells as a therapeutic option has not been examined so far.


The Werner syndrome helicase (WRN) plays a role in maintaining genomic stability. The lack of WRN results in Werner syndrome, a rare autosomal recessive genetic disorder, which causes premature aging accompanied by many complications such as rare forms of cancer and type 2 diabetes. However, the underlying mechanisms of these complications, arising due to the loss of WRN, are poorly understood. In this study, we demonstrated the function of WRN in transcriptional regulation of NF-kappaB targets. WRN physically interacts via its RecQ C-terminal (RQC) domain with the Rel homology domain of both the RelA (p65) and the p50 subunits of NF-kappaB. In the steady state, WRN is recruited to HIV-1 long terminal repeat (LTR), a typical NF-kappaB-responsive promoter, as well as the p50/p50 homodimer, in an NF-kappaB site-dependent manner. The amount of WRN on LTR increased along with the transactivating RelA/p50 heterodimer in response to TNF-alpha stimulation. Further, a knockdown of WRN reduced the transactivation of LTR in exogenous RelA/p50-introduced or TNF-alpha-stimulated cells. Additionally, knockdown of WRN reduced TNF-alpha stimulation-induced activation of the endogenous promoter of IL-8, an NF-kappaB-responsive gene, and WRN increased its association with the IL-8 promoter region together with RelA/p50 after TNF-alpha stimulation. In conjunction with studies that have shown NF-kappaB to be a key regulator of aging and inflammation, our results indicate a novel role of WRN in transcriptional regulation. Along with NF-kappaB, the loss of WRN is expected to result in incorrect regulation of downstream targets and leads to immune abnormalities and homeostatic disruption.


BACKGROUND: Biomarkers of inflammation and altered coagulation are of increasing interest as predictors of chronic disease and mortality in HIV patients, as well as the use of risk stratification scores such as the Framingham index and the Veterans Aging Cohort Study (VACS) score. METHODS: Demographic and laboratory data for 252 HIV patients were assessed for their relationship with 5 biomarkers: hsCRP, D-dimer, Cystatin C, IL-6 and TNF-alpha. Analysis of variance was used to model the association between the number of elevated biomarkers patients had and their Framingham 10 year cardiovascular risk and VACS scores. RESULTS: 87% of patients were male and 75.7% were virally suppressed (HIV RNA <48 copies/ml). The median and interquartile ranges for each biomarker were: hsCRP 1.65 ug/mL (0.73, 3.89), D-dimer 0.17 ug/mL (0.09, 0.31), Cystatin C 0.87 mg/L (0.78, 1.01), IL-6 2.13 pg/mL (1.3, 3.59), TNF-alpha 4.65 pg/mL (3.5, 5.97). 62.6% of patients had more than one biomarker >75th percentile, while 18.6% had three or more elevated biomarkers. Increased age, cigarette smoking, CD4 counts of <200 cells/mm3, Framingham scores and VACS scores were most strongly associated with elevations in biomarkers. When biomarkers were used to predict the Framingham and VACS scores, those with a higher number of elevated biomarkers had higher mean VACS scores, with a similar but less robust finding for Framingham scores. CONCLUSIONS: Despite viral suppression and
immunological stability, biomarkers of inflammation and coagulation remain elevated in a significant number of patients with HIV and are associated with higher scores on risk stratification indices.


Aging has been associated with increased generation of free radicals as well as immunosenescence. Previous studies have identified older individuals with inverted T CD4:CD8 cell ratio and increased immunity to cytomegalovirus (CMV). Here, we investigated markers of oxidative stress and antioxidant defences in older individuals with inverted CD4:CD8 T-cell ratio. Sixty-one subjects were identified with inverted CD4:CD8 ratio. Older individuals with a CD4:CD8 ratio <1 had increased levels of plasma advanced oxidation protein products (AOPP) and ferric reducing ability of plasma (FRAP), but reduced levels of thiobarbituric acid reactive substances (TBARS) as compared to subjects with normal CD4:CD8 ratio. The CMV IgG serology was negatively correlated with CD4:CD8 ratio. These markers were more evident among elderly men than women. Our data suggest a close relationship between chronic CMV infection and oxidative profile in older individuals in the midst of its influence on the peripheral T-cell subsets.


Both HIV infection and Methamphetamine (Meth) use disorders are associated with greater depressive symptoms and oxidative stress; whether the two conditions would show additive or interactive effects on the severity of depressive symptoms, and whether this is related to the level of oxidative stress in the CNS is unknown. 123 participants were evaluated, which included 41 HIV-seronegative subjects without substance use disorders (Control), 25 with recent (<6 months) moderate to severe Meth use disorders (Meth), 34 HIV-seropositive subjects without substance use disorders (HIV) and 23 HIV+Meth subjects. Depressive symptoms were assessed with the Center for Epidemiologic Studies-Depression Scale (CES-D), and oxidative stress markers were evaluated with glutathione (GSH), 4-hydroxynonenal (HNE), and activities of gamma-glutamyltransferase (GGT) and glutathione peroxidase (GPx) in the cerebrospinal fluid (CSF). Compared with Controls, HIV subjects had higher levels of HNE (+350%) and GGT (+27%), and lower level of GSH (-34%), while Meth users had higher levels of GPx activity (+23%) and GSH (+30 %). GGT correlated with GPx, and with age, across all subjects (p < 0.0001). CES-D scores correlated with CSF HNE levels only in Control and HIV groups, but not in Meth and HIV+Meth groups. HIV and Meth use had an interactive effects on depressive symptoms, but did not show additive or interactive effects on oxidative stress. The differential relationship between depressive symptoms and oxidative stress response amongst the four groups suggest that depressive symptoms in these groups are mediated through different mechanisms which are not always related to oxidative stress.


BACKGROUND: Bipolar disorder (BD) is commonly comorbid with many medical disorders including atopy, and appears characterized by progressive social, neurobiological, and functional impairment associated with increasing number of episodes and illness duration. Early and late stages of BD may present different biological features and may therefore require different treatment strategies. Consequently, the aim of this study was to evaluate serum levels of eotaxin/CCL11, eotaxin-2/CCL24, IL-2, IL-4, IL-6, IL-10, IL-17, TNF-alpha, IFNgamma, BDNF,
TBARS, carbonyl, and GPx in a sample of euthymic patients with BD at early and late stages compared to controls.

METHODS: Early-stage BD patients, 12 late-stage patients, and 25 controls matched for sex and age were selected. 10mL of peripheral blood was drawn from all subjects by venipuncture. Serum levels of BDNF, TBARS, carbonyl content, glutathione-peroxidase activity (GPx), cytokines (IL-2, IL-4, IL-6, IL-10, IL-17, TNF-alpha and IFNgamma), and chemokines (eotaxin/CCL11 and eotaxin-2/CCL24) were measured. RESULTS: There were no demographic differences between patients and controls. No significant differences were found for any of the biomarkers, except chemokine eotaxin/CCL11, whose serum levels were higher in late-stage patients with BD when compared to controls (p=0.022; Mann-Whitney U test). LIMITATIONS: Small number of subjects and use of medication may have influenced our results. CONCLUSION: The present study suggests a link between biomarkers of atopy and eosinophil function and bipolar disorder. These findings are also in line with progressive biological changes partially mediated by inflammatory imbalance, a process referred to as neuroprogression.


BACKGROUND: Recently, some systemic inflammation-based biomarkers have been demonstrated useful for predicting risk of death in patients with solid cancer independently of tumor characteristics. This study aimed to investigate the prognostic role of systemic inflammation-based biomarkers in HIV-infected patients with solid tumors and to propose a risk score for mortality in these subjects. METHODS: Clinical and pathological data on solid AIDS-defining cancer (ADC) and non-AIDS-defining cancer (NADC), diagnosed between 1998 and 2012 in an Italian cohort, were analyzed. To evaluate the prognostic role of systemic inflammation- and nutrition-based markers, univariate and multivariable Cox regression models were applied. To compute the risk score equation, the patients were randomly assigned to a derivation and a validation sample. RESULTS: A total of 573 patients (76.3% males) with a mean age of 46.2 years (SD = 10.3) were enrolled. 178 patients died during a median of 3.2 years of follow-up. For solid NADCs, elevated Glasgow Prognostic Score, modified Glasgow Prognostic Score, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and Prognostic Nutritional Index were independently associated with risk of death; for solid ADCs, none of these markers was associated with risk of death. For solid NADCs, we computed a mortality risk score on the basis of age at cancer diagnosis, intravenous drug use, and Prognostic Nutritional Index. The areas under the receiver operating characteristic curve were 0.67 (95% confidence interval: 0.58 to 0.75) in the derivation sample and 0.66 (95% confidence interval: 0.54 to 0.79) in the validation sample. CONCLUSIONS: Inflammatory biomarkers were associated with risk of death in HIV-infected patients with solid NADCs but not with ADCs.


Men with human immunodeficiency virus (HIV) infection are often hypogonadal and develop several HIV-associated non-acquired immunodeficiency syndrome (AIDS) (HANA) conditions that impair overall health status. No studies explored the relationship between health status and serum testosterone (T) in HIV-infected men. This study aims to investigate the association between total serum T and HANA, multimorbidity, and frailty in a large cohort of 1359 HIV-infected men and to explore the relationship between patients’ overall health status and serum T. Among biochemical and hormonal measurement performed the main are serum total T, free triiodothyronine (fT3), and luteinizing hormone. Other outcome measurements include anthropometry, assessment of comorbidities and disabilities, overall health status defined as the number of HANA and by the 38-item multimorbidity frailty index, anthropometry, and bone mineral density. The cumulative relative risk of comorbidities is increased in HIV-infected men with hypogonadism (p < 0.001) and hypogonadism is associated with several comorbidities. The prevalence of hypogonadism increases progressively with the increase of the number of comorbidities. Frailty index is inversely
related to serum total T (age-adjusted \( r = 0.298, r(2) = 0.089, p < 0.0001 \)). Serum ft3 levels are significantly lower in hypogonadal than eugonadal men (\( p = 0.022 \)). This suggests that low serum T could be considered a sensitive marker of frailty and poor health status and that the latter might induce hypogonadism. The more HIV-infected men are frail the more they are hypogonadal. This suggests that hypogonadism might be a naturally occurring condition in unhealthy HIV-infected men and raises concern about the safety of T treatment. In conclusion, low serum T is associated with multimorbidity, HANA, and frailty in HIV-infected men and this association seems to be bidirectional. Given the wide attitude to offer T treatment to HIV-infected men, caution is needed when prescribing T to HIV-infected male patients, especially if the patient is unhealthy or frail.


Frailty is a complex and heterogeneous clinical syndrome. Cognitive frailty has been considered as a subtype of frailty. In this study, we refine the definition of cognitive frailty based on existing reports about frailty and the latest progress in cognition research. We obtain evidence from the literature regarding the role of pre-physical frailty in pathological aging. We propose that cognitive impairment of cognitive frailty results from physical or pre-physical frailty and comprises two subtypes: the reversible and the potentially reversible. Reversible cognitive impairment is indicated by subjective cognitive decline (SCD) and/or positive fluid and imaging biomarkers of amyloid-beta accumulation and neurodegeneration. Potentially reversible cognitive impairment is MCI (CDR=0.5). Based on the severity of cognitive impairment, it is possible to determine the primary and secondary preventative measures for cognitive frailty. We further determine whether SCD is a component of pre-clinical AD or the early stage of other neurodegenerative diseases, which is required for guiding personal clinical intervention.


OBJECTIVE: Social control in the health domain refers to attempts by social network members to get an individual to modify their health behaviors. According to the dual effects model of social control, having one's health behavior controlled by others should be related to healthier behavioral change, but might arouse psychological distress as one may resent being controlled. Despite potential healthy behavior change, the stress of social control may thus be detrimental as interpersonal stress has been related to negative health outcomes. In the present study, the association between perceived social control and telomere length was tested to examine its association to biological outcomes. METHOD: In this cross-sectional study, a relatively healthy community sample of 140 middle age and older adults completed measures of perceived social control, perceived stress, and health behaviors. Peripheral blood mononuclear cells were used to determine telomere length. RESULTS: Main results showed that higher levels of perceived direct social network control were associated with shorter telomere length. These links were not influenced by statistical controls for medication use, self-rated health, trait hostility, and optimism. Perceived social control was also related to greater perceived stress but not health behaviors overall. However, neither perceived stress nor health behaviors mediated the link between social control and telomere length. CONCLUSIONS: Although the study design precludes strong inferences, these results suggest that perceived social control may be associated with cellular aging. These data also highlight the utility of integrating biological outcomes into social control models. (PsycINFO Database Record

Combination antiretroviral therapy transformed human immunodeficiency virus (HIV)-infection from a terminal illness to a manageable condition, but these patients remain at a significantly elevated risk of developing cognitive impairments and the mechanisms are not understood. Some previous neuroimaging studies have found hyperactivation in frontoparietal networks of HIV-infected patients, whereas others reported aberrations restricted to sensory cortices. In this study, we utilize high-resolution structural and neurophysiological imaging to determine whether alterations in brain structure, function, or both contribute to HIV-related cognitive impairments. HIV-infected adults and individually matched controls completed 3-Tesla structural magnetic resonance imaging (sMRI) and a mechanoreception task during magnetoencephalography (MEG). MEG data were examined using advanced beamforming methods, and sMRI data were analyzed using the latest voxel-based morphometry methods with DARTEL. We found significantly reduced theta responses in the postcentral gyrus and increased alpha activity in the prefrontal cortices of HIV-infected patients compared with controls. Patients also had reduced gray matter volume in the postcentral gyrus, parahippocampal gyrus, and other regions. Importantly, reduced gray matter volume in the left postcentral gyrus was spatially coincident with abnormal MEG responses in HIV-infected patients. Finally, left prefrontal and postcentral gyrus activity was correlated with neuropsychological performance and, when used in conjunction, these two MEG findings had a sensitivity and specificity of over 87.5% for HIV-associated cognitive impairment. This study is the first to demonstrate abnormally increased activity in association cortices with simultaneously decreased activity in sensory areas. These MEG findings had excellent sensitivity and specificity for HIV-associated cognitive impairment, and may hold promise as a potential disease marker.


BACKGROUND: Both HIV infection and frailty have been associated with chronic immune activation. One possible explanation for this chronic immune activation could be low levels of CD4(+) T regulatory cells (Tregs), which suppress immune responses. METHODS: HIV-uninfected (HIV-) and HIV-infected (HIV+) men in the Multicenter AIDS Cohort Study (MACS) were classified as frail (or nonfrail) if they expressed (or did not express) the Fried frailty phenotype at two consecutive study visits. Percentages and absolute numbers of total Tregs, and percentages of different subsets of Tregs and of activated T cells were measured by flow cytometry. The function of Tregs was measured by suppression of T-cell proliferation. RESULTS: Percentages of Tregs were higher, rather than lower, in frail men than in nonfrail men, and this difference was significant for HIV- men. Percentages of subsets of Tregs did not differ significantly by frailty status. Among HIV+ men, the suppressive function of Tregs was similar between frail and nonfrail men. Percentages of Tregs and activated T cells were negatively correlated in nonfrail men (HIV- and HIV+) and in frail HIV- men, but this correlation was strongly positive in frail HIV+ men. CONCLUSION: These data suggest that: (a) Tregs were not deficient in frail men; and (b) the immunological pathophysiology of frailty may differ by HIV status.

Comorbidities

(S008) The Impact of HPV, HIV, and Smoking on Oncologic and Functional Outcomes in Patients With Head and Neck Cancer." Oncology (Williston Park) 29(4 Suppl 1).

Patients with HIV may have an increased risk of hypertension and cardiovascular disease (CVD). The objective of this study was to determine the prevalence and risk factors for hypertension in a population of HIV-infected patients at an HIV/AIDS clinic in southern Brazil. We reviewed medical records of 1009 HIV-infected patients aged 18 years or more in an urban HIV/AIDS clinic based in Porto Alegre, southern Brazil. Hypertension was defined according to the Eighth Joint National Committee criteria. The prevalence of hypertension in this study cohort was 22.5% (95% confidence interval, 20%-25.2%). Individuals were significantly older in the hypertensive group (P < .001). After adjustment using a Poisson regression model of all variables that presented P < .2 in the univariate analysis, the variables that were significantly associated with hypertension were only age >/=40 years and obesity. Also in this setting, dyslipidemia (P = .068) showed a tendency of association with hypertension. Compared with HIV-infected persons aged 18-39 years, those aged 40-59 years presented a 2-fold higher prevalence of hypertension (95% confidence interval, 1.2-3.3). The present study showed a high prevalence of hypertension among HIV-infected persons, similar to other studies, ranging from 13% to 45%, and also similar to the HIV-negative general population. Age and obesity were the factors associated with hypertension. Finally, the present study indicates a similar pattern of behavior and comorbidities for HIV-positive and -negative patients in relation to hypertension.


BACKGROUND: Pulmonary infections remain more common in HIV-infected (HIV+) compared with uninfected individuals. The increase in chronic lung diseases among aging HIV+ individuals may contribute to this persistent risk. We sought to determine whether chronic obstructive pulmonary disease (COPD) is an independent risk factor for different pulmonary infections requiring hospitalization among HIV+ patients. METHODS: We analyzed data from 41,993 HIV+ Veterans in the nationwide Veterans Aging Cohort Study Virtual Cohort from 1996 to 2009. Using International Classification of Diseases, Ninth Revision codes, we identified baseline comorbid conditions, including COPD, and incident community-acquired pneumonia (CAP), pulmonary tuberculosis (TB), and Pneumocystis jirovecii pneumonia (PCP) requiring hospitalization within 2 years after baseline. We used multivariable Poisson regression to determine incidence rate ratios (IRRs) associated with COPD for each type of pulmonary infection, adjusting for comorbidities, CD4 cell count, HIV viral load, smoking status, substance use, vaccinations, and calendar year at baseline. RESULTS: Unadjusted incidence rates of CAP, TB, and PCP requiring hospitalization were significantly higher among persons with COPD compared to those without COPD (CAP: 53.9 vs. 19.4 per 1000 person-years; TB: 8.7 vs. 2.8; PCP: 15.5 vs. 9.2; P </.= 0.001). In multivariable Poisson regression models, COPD was independently associated with increased risk of CAP, TB, and PCP (IRR: 1.94, 95% confidence interval [CI]: 1.64 to 2.30; IRR: 2.60, 95% CI: 1.70 to 3.97; and IRR: 1.48, 95% CI: 1.10 to 2.01, respectively). CONCLUSIONS: COPD is an independent risk factor for CAP, TB, and PCP requiring hospitalization among HIV+ individuals. As the HIV+ population ages, the growing burden of COPD may confer substantial risk for pulmonary infections.


Human Immunodeficiency Virus- (HIV-) infected persons have a higher risk for acute myocardial infarction (AMI) than HIV-uninfected persons. Earlier studies suggest that HIV viral load, CD4+ T-cell count, and antiretroviral therapy are associated with cardiovascular disease (CVD) risk. Whether CD8+ T-cell count is associated with CVD risk is not clear. We investigated the association between CD8+ T-cell count and incident AMI in a cohort of 73,398 people (of which 97.3% were men) enrolled in the U.S. Veterans Aging Cohort Study-Virtual Cohort (VACS-VC). Compared to uninfected people, HIV-infected people with high baseline CD8+ T-cell counts (>1065 cells/mm3) had increased AMI risk (adjusted HR=1.82, P<0.001, 95% CI: 1.46 to 2.28). There was evidence that the effect of CD8+ T-cell tertiles on
AMI risk differed by CD4+ T-cell level: compared to uninfected people, HIV-infected people with CD4+ T-cell counts $\geq$ 200 cells/mm$^3$ had increased AMI risk with high CD8+ T-cell count, while those with CD4+ T-cell counts < 200 cells/mm$^3$ had increased AMI risk with low CD8+ T-cell count. CD8+ T-cell counts may add additional AMI risk stratification information beyond that provided by CD4+ T-cell counts alone.


The 18th WHO Global Tuberculosis Annual Report indicates that there were an estimated 8.6 million incident cases of tuberculosis (TB) in 2012, which included 2.9 million women and 530,000 children. TB caused 1.3 million deaths including 320,000 human immunodeficiency virus (HIV)-infected people; three-quarters of deaths occurred in Africa and Southeast Asia. With one-third of the world’s population latently infected with Mycobacterium tuberculosis (Mtbt), active TB disease is primarily associated with a break down in immune surveillance. This explains the strong link between active TB disease and other communicable diseases (CDs) or noncommunicable diseases (NCDs) that exert a toll on the immune system. Comorbid NCD risk factors include diabetes, smoking, malnutrition, and chronic lung disease, all of which have increased relentlessly over the past decade in developing countries. The huge overlap between killer infections such as TB, HIV, malaria, and severe viral infections with NCDs, results in a "double burden of disease" in developing countries. The current focus on vertical disease programs fails to recognize comorbidities or to encourage joint management approaches. This review highlights major disease overlaps and discusses the rationale for better integration of tuberculosis care with services for NCDs and other infectious diseases to enhance the overall efficiency of the public health responses.


Successful combination therapy for human immunodeficiency virus (HIV) has transformed this disease from a short-lived infection with high mortality to a chronic disease associated with increasing life expectancy. This is true for high- as well as low- and middle-income countries. As a result of this increased life expectancy, people living with HIV are now at risk of developing other chronic diseases associated with aging. Heart failure has been common among people living with HIV in the eras of pre- and post- availability of antiretroviral therapy; however, our current understanding of the pathogenesis and approaches to management have not been systematically addressed. HIV may cause heart failure through direct (e.g., viral replication, mitochondrial dysfunction, cardiac autoimmunity, autonomic dysfunction) and indirect (e.g., opportunistic infections, antiretroviral therapy, alcohol abuse, micronutrient deficiency, tobacco use) pathways. In low- and middle-income countries, 2 large observational studies have recently reported clinical characteristics and outcomes in these patients. HIV-associated heart failure remains a common cardiac diagnosis in people living with heart failure, yet a unifying set of diagnostic criteria is lacking. Treatment patterns for heart failure fall short of society guidelines. Although there may be promise in cardiac glycosides for treating heart failure in people living with HIV, clinical studies are needed to validate in vitro findings. Owing to the burden of HIV in low- and middle-income countries and the concurrent rise of traditional cardiovascular risk factors, strategic and concerted efforts in this area are likely to impact the care of people living with HIV around the globe.


OBJECTIVE: We aimed at assessing in persons living with HIV with a smoking history an association between lung cancer risk and protease inhibitors exposure, especially ritonavir. DESIGN: A nested case-control study was conducted within the ANRS CO4 FHDH, CO3 Aquitaine and Tenon's Hospital Cohorts. METHODS: Cases and controls were eligible if they were ex-smokers or current smokers at the index date, and had a CD4 cell count reported in the year preceding the index date. Cases were incident cases of lung cancer diagnosed between 1 January 2000 and 31 December 2011. All cancer cases were validated and histological types identified when available. Three controls were randomly selected by incidence density sampling using calendar time as the time axis, with individual matching on cohort, age (+/- 5 years), route of HIV acquisition, sex and hospital. Analyses were performed using conditional logistic regression adjusted for nadir CD4 cell count and smoking status. Ritonavir and protease inhibitors exposures were represented in separate models using categorical variables (never exposed, ever exposed). Several sensitivity analyses were performed. RESULTS: This study performed in 1447 persons living with HIV with a smoking history (383 lung cancer cases and 1064 control patients) did not evidence any association between lung cancer risk and protease inhibitors exposure including ritonavir. CONCLUSION: These results suggest that the risk of lung cancer is not influenced by pharmacologically induced P450 cytochrome protease inhibitors inhibition among smokers or ex-smokers.


OBJECTIVES: The aim of the study was to estimate the cumulative incidence of, and rates of progression to, invasive anal cancer (IAC) according to baseline anal cytology screening category in an unselected HIV clinical care cohort in the antiretroviral era. METHODS: A retrospective cohort analysis of HIV-infected patients under care at the University of California at San Diego Owen Clinic was carried out. Patients were eligible for this analysis if they had at least two anal cytohistological results available for longitudinal analysis. Kaplan-Meier analysis was used to estimate the cumulative incidence of IAC over time according to baseline cytology category [less than high-grade intraepithelial lesion (HSIL) versus HSIL]. Cox regression analysis was used to adjust for the following covariates: antiretroviral use, level of HIV viraemia, smoking status and infrared photocoagulation (IRC) ablation therapy. RESULTS: Between 2000 and 2012, we followed 2804 HIV-infected patients for a median of 4 years under a clinic protocol requiring baseline anal cytology screening. Incident IAC was diagnosed in 23 patients. Patients with a baseline HSIL anal cytology had an estimated 5-year probability of progression to IAC of 1.7% and an estimated annual progression risk of 1 in 263. None of the examined covariates was significantly associated with IAC incidence when examined in separate unadjusted Cox models. CONCLUSIONS: HIV-infected patients with a baseline HSIL anal cytology had a 5-year cumulative incidence of IAC of 1.65%, with an upper 95% confidence bound of 4.5%. This population-based study provides quantitative risk estimates that may be used for counselling patients regarding management options for abnormal cytology results.


Washington, DC (DC), has among the highest AIDS prevalence and cancer incidence in the USA. This study compared cancer diagnoses and survival among AIDS cases with AIDS-defining cancers (ADCs) to those with non-AIDS-defining cancers (NADCs) in DC from 1996 to 2006. Survival by cancer type and time period was also examined for 300 individuals diagnosed with AIDS who developed cancer; 49% of AIDS cases developed an ADC. ADC cases were younger at both AIDS and cancer diagnosis and had significantly lower median CD4 counts at AIDS diagnosis than
NADC cases. The most frequent cancers were non-Hodgkin lymphoma (NHL; 44% of ADC), Kaposi’s sarcoma (40% of ADC), and lung cancer (20% of NADC). There was no significant difference in distribution of cancers when comparing ADCs to NADCs, or over time (1996-2001 vs. 2002-2006). Survival among NHL, oral cavity, and lung cancer cases was 0.4, 0.8, and 0.3 years, respectively; the risk of death was approximately two times higher for each of these cancers when compared to other cancers. Given the high burden of cancer and HIV in DC, early highly active antiretroviral therapy initiation, routine cancer screening, and risk reduction through behavioral modification should be emphasized to prevent cancer among HIV-infected persons.


OBJECTIVES: Non-AIDS-related malignancies now represent a frequent cause of death among HIV-infected patients. Albeit bladder cancer is one of the most common malignancies worldwide, it has been rarely reported among HIV-infected patients. We wished to assess the prevalence and characteristics of bladder cancer in HIV-infected patients. METHODS: We conducted a single center retrospective study from 1998 to 2013 in a university hospital in Paris. Cases of bladder cancer among HIV-infected patients were identified using the electronic records of the hospital database and of the HIV-infected cohort. Patient characteristics and outcomes were retrieved from patients charts. A systematic review of published cases of bladder cancers in patients with HIV-infection was also performed. RESULTS: During the study period we identified 15 HIV-infected patients (0.2% of the cohort) with a bladder cancer. Patients were mostly men (73%) and smokers (67%), with a median age of 56 years at cancer diagnosis. Bladder cancer was diagnosed a median of 14 years after HIV-infection. Most patients were on ART (86%) with median current and nadir CD4 cell counts of 506 and 195 cells/mm3, respectively. Haematuria (73%) was the most frequent presenting symptom and HPV-associated lesions were seen in 6/10 (60%) patients. Histopathology showed transitional cell carcinoma in 80% and a high proportion of tumors with muscle invasion (47%) and high histologic grade (73%). One-year survival rate was 74.6%. The systematic review identified 13 additional cases of urothelial bladder cancers which shared similar features. CONCLUSIONS: Bladder cancers in HIV-infected patients remain rare but may occur in relatively young patients with a low nadir CD4 cell count, have aggressive pathological features and can be fatal.


PURPOSE: Despite advances in the treatment of HIV, HIV-infected people remain at increased risk for many cancers, and the number of non-AIDS-defining cancers is increasing with the aging of the HIV-infected population. No prior study has comprehensively evaluated the effect of HIV on cancer-specific mortality. PATIENTS AND METHODS: We identified cases of 14 common cancers occurring from 1996 to 2010 in six US states participating in a linkage of cancer and HIV/AIDS registries. We used Cox regression to examine the association between patient HIV status and death resulting from the presenting cancer (ascertained from death certificates), adjusting for age, sex, race/ethnicity, year of cancer diagnosis, and cancer stage. We included 1,816,461 patients with cancer, 6,459 (0.36%) of whom were HIV infected. RESULTS: Cancer-specific mortality was significantly elevated in HIV-infected compared with HIV-uninfected patients for many cancers: colorectum (adjusted hazard ratio [HR], 1.49; 95% CI, 1.21 to 1.84), pancreas (HR, 1.71; 95% CI, 1.35 to 2.18), larynx (HR, 1.62; 95% CI, 1.06 to 2.47), lung (HR, 1.28; 95% CI, 1.17 to 1.39), melanoma
(HR, 1.72; 95% CI, 1.09 to 2.70), breast (HR, 2.61; 95% CI, 2.06 to 3.31), and prostate (HR, 1.57; 95% CI, 1.02 to 2.41). HIV was not associated with increased cancer-specific mortality for anal cancer, Hodgkin lymphoma, or diffuse large B-cell lymphoma. After further adjustment for cancer treatment, HIV remained associated with elevated cancer-specific mortality for common non-AIDS-defining cancers: colorectum (HR, 1.40; 95% CI, 1.09 to 1.80), lung (HR, 1.28; 95% CI, 1.14 to 1.44), melanoma (HR, 1.93; 95% CI, 1.14 to 3.27), and breast (HR, 2.64; 95% CI, 1.86 to 3.73).

CONCLUSION: HIV-infected patients with cancer experienced higher cancer-specific mortality than HIV-uninfected patients, independent of cancer stage or receipt of cancer treatment. The elevation in cancer-specific mortality among HIV-infected patients may be attributable to unmeasured stage or treatment differences as well as a direct relationship between immunosuppression and tumor progression.


BACKGROUND: Adding gender-related modifiable characteristics or behaviors to the Veterans Aging Cohort Study (VACS) index might improve the accuracy of predicting mortality among HIV-infected women on treatment. We evaluated the VACS index in women with HIV, determined whether additional variables would improve mortality prediction, and quantified the potential for improved survival associated with reduction in these additional risk factors. METHODS: The VACS index (based on age, CD4 count, HIV-1 RNA, hemoglobin, aspartate aminotransferase, alanine aminotransferase, platelets, creatinine, and Hepatitis C status) was validated in HIV-infected women in the Women's Interagency HIV Study (WIHS) who initiated antiretroviral therapy between January 1996 and December 2007. Models were constructed adding race, depression, abuse, smoking, substance use, transactional sex, and comorbidities to determine whether predictability improved. Population attributable fractions were calculated.

RESULTS: The VACS index accurately predicted 5-year mortality in 1057 WIHS women with 1 year on highly active antiretroviral therapy with c-index 0.83 [95% confidence interval (CI): 0.79 to 0.87]. In multivariate analysis, the VACS index score [adjusted hazard ratio (aHR) for a 5-point increment 1.30; 95% CI: 1.25 to 1.35], depressive symptoms (aHR 1.73; 95% CI: 1.17 to 2.56), and history of transactional sex (aHR 1.93; 95% CI: 1.33 to 1.82) were independent statistically significant predictors of mortality. CONCLUSIONS: Both depression and transactional sex significantly improved the performance of the VACS index in predicting mortality among HIV-infected women. Providing treatment for depression and addressing economic and psychosocial instability in HIV-infected women would improve health and perhaps point to a broader public health approach to reducing HIV mortality.


Marked improvements in survival and health outcome for people infected with HIV have occurred since the advent of combination antiretroviral therapy over a decade ago. Yet HIV-associated neurocognitive disorders continue to occur with an alarming prevalence. This may reflect the fact that infected people are now living longer with chronic infection. There is mounting evidence that HIV exacerbates age-associated cognitive decline. Many middle-aged HIV-infected people are experiencing cognitive decline similar to that found among much older adults. An increased prevalence of vascular and metabolic comorbidities has also been observed and is greatest among older adults with HIV. Premature age-associated neurocognitive decline appears to be related to structural and functional brain changes on neuroimaging, and of particular concern is the fact that pathology indicative of neurodegenerative disease has been shown to occur in the brains of HIV-infected people. Yet notable differences also exist between the clinical presentation and brain disturbances occurring with HIV and those occurring in neurodegenerative conditions such as Alzheimer's disease. HIV interacts with the aging brain to affect neurological structure and function. However, whether this interaction directly affects neurodegenerative processes, accelerates
normal cognitive aging, or contributes to a worsening of other comorbidities that affect the brain in older adults remains an open question. Evidence for and against each of these possibilities is reviewed.


Background: HIV-1 infection is well-controlled using combination anti-retroviral therapy (cART). Nevertheless, HIV patients may remain at increased risk of cognitive decline, motor impairment and susceptibility to dementia, along with other age-associated comorbidities. Cross-sectional and longitudinal neuroimaging shows structural brain changes in HIV patients similar to those seen in older healthy individuals, suggesting that HIV infection may accelerate brain ageing, despite successful management with cART. This study aimed to compare HIV patients to a model of healthy brain ageing to examine whether the disease affected ‘brain age’.

Methods: Employing a machine learning approach that allows accurate prediction of age using structural brain images, defined on a large independent dataset of healthy individuals (n = 1537), the brain age of HIV-1 patients and controls was estimated. The sample consisted of 106 HIV patients with suppressed viremia on cART for ≥ 12 months (mean age 56.82 ± 7.78 years, 102 males, 4 females) and 58 uninfected controls (57.73 ± 7.83 years, 56 males, 2 females; and comparable regarding ethnicity, sexual orientation, premorbid intelligence, and educational level) recruited at two sites (Amsterdam and London). The analysis was conducted separately on grey and white matter images and the predicted age difference (PAD) between predicted and chronological age was calculated, generating a measure that captures multivariate elements of brain structure. Group differences were then explored using analysis of covariance, adjusting for chronological age and study site.

Results: Grey matter in HIV patients showed premature ageing, with a mean PAD score of 9.2 (95% CI 7.7, 10.7) years, which was significantly greater than in controls (P = 0.02). However, controls also had evidence of grey matter ageing effects (PAD = 6.1 years, 95% CI 3.7, 8.5). White matter was also older in HIV patients, but to a lesser extent (PAD = 1.6 years, 95% CI 0.4, 2.9). This was not significantly different from the control group (P = 0.7), which showed similar effects (PAD = 1.23 years, 95% CI – 0.7, 3.19).

Conclusions: HIV patients had evidence of prematurely aged grey matter compared to controls who themselves also showed increased ageing compared to an independent reference cohort. However, changes in these groups were less pronounced for white matter. These preliminary results may support the idea of premature brain ageing underlying the increased risk of cognitive decline reported in HIV patients. Further analyses are needed to distinguish the contribution from HIV-associated and other recognized risk factors. The contrasting patterns of ageing between grey and white matter may give insights into pathological processes at work, as well as differentiating from other clinical samples that show distinct patterns of brain ageing.


With the development of effective antiretroviral therapy, HIV-infected women are living longer and transitioning through menopause. The purpose of our study was to systematically examine the evidence that menopause is an additional risk predictor for osteoporosis and fractures in HIV-infected women. Electronic databases
were searched for studies of low bone density or fractures in HIV-infected postmenopausal women. Studies that met the inclusion criteria (n = 10) were appraised using a validated quality assessment tool. The majority of studies were rated as good quality and the remaining were fair. The prevalence of osteoporosis reported in these studies ranged from 7.3% to 84% and 0.7% to 23% in HIV-infected and uninfected postmenopausal women, respectively. In the two qualifying studies, postmenopausal status was not a predictor of fractures in HIV-infected women. Findings suggest that HIV care providers should accurately assess postmenopausal status and modifiable risk factors for osteoporosis in all older HIV-infected women.


OBJECTIVE: To evaluate the prevalence of anal cytology (ACyt) abnormalities among HIV-infected and HIV-uninfected men who have sex with men (MSM) DESIGN: Multicenter cohort study of 723 HIV-infected and 788 HIV-uninfected MSM with ACyt, with a second ACyt collected two years later. Referral for high-resolution anoscopy (HRA) was suggested for abnormal ACyt. METHODS: ACyt samples were collected using a polyester swab and liquid cytology media, and read in a central laboratory. RESULTS: Prevalence of any abnormal ACyt was 25% in HIV-uninfected MSM, and increased to 38%, 41%, and 47% among HIV-infected MSM with current CD4+ T-cell counts >/=500, 350-499, and <350 cells/mm (p<0.001), respectively. Anal HPV16 DNA was also more common in HIV-infected than HIV uninfected MSM (25% vs 16%, p<0.001). Abnormal baseline ACyt together with prevalent HPV16 DNA detection was present in only 7% of HIV-uninfected MSM compared to 18% of HIV-infected MSM with current CD4<350, p<0.001). Among HIV-infected men, 56% of the men with low grade squamous intraepithelial lesions ASC-US/LSIL and 81% of men with atypical squamous cells cannot exclude high grade (ASC-H)/high grade SIL (HSIL) had lower grade ACyt findings 18-30 months later ("regressed"). However, 19% of untreated HIV-infected men with ASC-H/HSIL cytology maintained that same grade of cytology at their second test approximately two years later, and 15% with ASC-US/LSIL "progressed" to ASC-H/HSIL. Abnormal ACyt had high sensitivity (96%) but low specificity (17%) for biopsy proven HSIL.

CONCLUSIONS: Prevalence of abnormal ACyt remains elevated in HIV-infected men during the current ART era.


OBJECTIVE: HIV-infected people are at increased risk of cancers of infectious origin. We estimated the burden of cancer attributable to infections among HIV-infected people in the United States in 2008. DESIGN: Incidence rates for cancer sites associated with infections were estimated from record linkage between HIV/AIDS registries and cancer registries. METHODS: Rates were applied to estimates of the population living with diagnosed HIV in the United States in 2008 to obtain the number of incident cancer cases. Site-specific attributable fractions and corresponding 95% confidence intervals (CIs) were estimated from infection prevalence among cancer cases. Infection prevalence data were derived from literature review of case series. RESULTS: Of an estimated 6200 incident cancer cases (95% CI 6000-6500), 2500 (95% CI 2400-2700) were attributable to infection (attributable fraction = 40%, 95% CI 39-42). The most important infections were Kaposi sarcoma herpes virus, Epstein-Barr virus, and human papillomavirus, which together were responsible for 2200 new cancer cases (95% CI 2100-2400), mainly Kaposi sarcoma, lymphomas, and ano-genital cancers. The attributable fraction in HIV-infected people was highest in the age group 20-29 years (69%, 95% CI 65-72). MSM were the HIV transmission group with the highest attributable fraction (48%, 95% CI 46-50), due to the high incidence of both Kaposi sarcoma and anal cancer. CONCLUSION: The very high fraction of cancer attributable to infection in HIV-infected people points to special opportunities to prevent these cancers, that is, avoidance, detection, and early treatment of cancer-associated infections, and universal early detection and uninterrupted treatment of HIV infection to avoid immunosuppression.

Recent advances in highly active anti-retroviral therapy (HAART) in their various combinations have dramatically increased the life expectancies of HIV-infected persons. People diagnosed with HIV are living beyond the age of 50 but are experiencing the cumulative effects of HIV infection and aging on brain function. In HIV-infected aging individuals, the potential synergy between immunosenescence and HIV viral loads increases susceptibility to HIV-related brain injury and functional brain network degradation similar to that seen in Parkinson's disease (PD), the second most common neurodegenerative disorder in the aging population. Although there are clear diagnostic differences in the primary pathology of both diseases, i.e., death of dopamine-generating cells in the substantia nigra in PD and neuroinflammation in HIV, neurotoxicity to dopaminergic terminals in the basal ganglia (BG) has been implied in the pathogenesis of HIV and neuroinflammation in the pathogenesis of PD. Similar to PD, HIV infection affects structures of the BG, which are part of interconnected circuits including mesocorticolimbic pathways linking brainstem nuclei to BG and cortices subserving attention, cognitive control, and motor functions. The present review discusses the combined effects of aging and neuroinflammation in HIV individuals on cognition and motor function in comparison with age-related neurodegenerative processes in PD. Despite the many challenges, some HIV patients manage to age successfully, most likely by redistribution of neural network resources to enhance function, as occurs in healthy elderly; such compensation could be curtailed by emerging PD.


OBJECTIVE: Antiretrovirals do not prevent anal intraepithelial neoplasia. However, the influence of antiretrovirals in the natural history of invasive anal cancer is less clear. The objective is to investigate the impact of antiretrovirals in the time to the development of anal cancer in HIV-positive MSM. DESIGN: A retrospective analysis of cases of anal cancer in a cohort of HIV-positive MSM receiving antiretrovirals between 1988 and 2008. METHODS: Time from first CD4 cell count or HIV RNA viral load test to anal cancer diagnosis was analysed using Cox regression and Kaplan-Meier curves. Anal cancer cases treated in the era prior to HAART (<1996) were compared with those treated later (1996-2008). RESULTS: Anal cancer cases (n = 37) were compared with a cohort of 1654 HIV-positive MSM on antiretrovirals. Antiretrovirals were started in the pre-HAART era by 70% of cancer cases, and median CD4 cell count nadir was 70 cells/mul (10-130). Time to development of anal cancer was shorter for cases treated during the pre-HAART era [adjusted hazard ratio (AHR) 3.04, 95% confidence interval (95% CI) 1.48-6.24, P = 0.002], with a CD4 cell count nadir less than 100 cells/mul (AHR 2.21, 95% CI 1.06-4.62, P = 0.035) and longer duration of CD4 cell count less than 100 cells/mul (AHR 1.33, 95% CI 1.11-1.58, P = 0.002). CONCLUSION: Results show that severe immunosuppression and starting therapy pre-HAART are associated with an increased risk of anal cancer. HIV-positive MSM initiating antiretrovirals during the HAART era (1996-2008) had a longer time to the development of anal cancer than those treated pre-HAART. Our results suggest that early use of HAART may delay progression to anal cancer.


OBJECTIVE: Older adults are increasingly likely to have two or more chronic medical conditions (multimorbidity) and are consequently at greater risk of disability. Here we examine the role of inflammation in mediating the relationship between multimorbidity and disability. METHOD: Data are from the Survey of Mid-Life in the United States (MIDUS), a national sample of middle-aged and older adults. Structural equation models were used to assess direct relationships between multimorbidity and activities of daily living as well as indirect associations with
a latent variable for inflammation (indicated by circulating levels of interleukin-6, C-reactive protein, and fibrinogen) as a mediator. RESULTS: After adjustment for potential confounds, multimorbidity was positively associated with inflammation ($p < .001$) and functional limitations ($p < .001$), and inflammation partially mediated the link between multimorbidity and functional limitations ($p < .01$). DISCUSSION: Inflammation may be an important biological mechanism through which chronic medical conditions are linked to disability in later life.


BACKGROUND: Geriatric syndromes such as falls, frailty, and functional impairment are multifactorial conditions used to identify vulnerable older adults. Limited data exist on these conditions in older HIV-infected adults, and no studies have comprehensively examined these conditions. METHODS: Geriatric syndromes including falls, urinary incontinence, functional impairment, frailty, sensory impairment, depression, and cognitive impairment were measured in a cross-sectional study of HIV-infected adults aged 50 years and older who had an undetectable viral load on antiretroviral therapy. We examined both HIV and non-HIV-related predictors of geriatric syndromes including sociodemographics, number of comorbidities and nonantiretroviral medications, and HIV-specific variables in multivariate analyses. RESULTS: We studied 155 participants with a median age of 57 (interquartile range: 54-62) and 94% were men. Prefrailty (56%), difficulty with instrumental activities of daily living (46%), and cognitive impairment (47%) were the most frequent geriatric syndromes. Lower CD4 nadir incidence rate ratio [IRR: 1.16, 95% (confidence interval) CI: 1.06 to 1.26], non-white race (IRR: 1.38, 95% CI: 1.10 to 1.74), and increasing number of comorbidities (IRR: 1.09, 95% CI: 1.03 to 1.15) were associated with increased risk of having more geriatric syndromes. CONCLUSIONS: Geriatric syndromes are common in older HIV-infected adults. Treatment of comorbidities and early initiation of antiretroviral therapy may help to prevent development of these age-related complications. Clinical care of older HIV-infected adults should consider incorporation of geriatric principles.


BACKGROUND: Individuals infected with human immunodeficiency virus (HIV) live longer as a result of effective treatment, but long-term consequences of infection, treatment, and immunological dysfunction are poorly understood. METHODS: We prospectively examined 1011 women (74% HIV-infected) in the Women's Interagency HIV Study and 811 men (65% HIV-infected) in the Multicenter AIDS Cohort Study who underwent repeated B-mode carotid artery ultrasound imaging in 2004-2013. Outcomes included changes in right common carotid artery intima-media thickness (CCA-IMT) and new focal carotid artery plaque formation (IMT >1.5 mm) over median 7 years. We assessed the association between HIV serostatus and progression of subclinical atherosclerosis, adjusting for demographic, behavioral, and cardiometabolic risk factors. RESULTS: Unadjusted mean CCA-IMT increased (725 to 752 microm in women, 757 to 790 microm in men), but CCA-IMT progression did not differ by HIV serostatus, either in combined or sex-specific analyses. Focal plaque prevalence increased from 8% to 15% in women and 25% to 34% in men over 7 years. HIV-infected individuals had 1.6-fold greater risk of new plaque formation compared with HIV-uninfected individuals (relative risk [RR] 1.61, 95% CI, 1.12-2.32), adjusting for cardiometabolic factors; the association was similar by sex. Increased plaque occurred even among persistently virologically suppressed HIV-infected individuals compared with uninfected individuals (RR 1.56, 95% CI, 1.07-2.27). HIV-infected individuals with
baseline CD4+ \( \geq 500 \) cells/microL had plaque risk not statistically different from uninfected individuals.

CONCLUSIONS: HIV infection is associated with greater increases in focal plaque among women and men, potentially mediated by factors associated with immunodeficiency or HIV replication at levels below current limits of detection.


INTRODUCTION: The total number of patients with Human Immunodeficiency Virus (HIV) is 33 million, with 2.7 million new infections in 2007(1). Puerto Rico has an increasing prevalence trend of Diabetes Mellitus of 12.8% in 2010(3). As treatment of HIV continues to develop, and access to therapy improves, the incidence of HIV associated diabetes is bound to grow. We investigate the prevalence of Diabetes Mellitus and its associated risk factors in a determinate HIV positive population. MATERIALS AND METHODS: A retrospective study, reviewing the medical records of 146 HIV positive patients. The prevalence of DM was statistically measured and a Logistic Regression with Pearson Chi2 Square and Fisher’s exact test was used to assess the association between DM and its risks factors.

RESULTS: The prevalence of DM in the studied population was 13.7% (n=20). There were 59% (n = 86) males, 43% (n = 63) of patients treated with HAART 46% (n = 67) IVDA, the mean age was 47; with 29% older than 50 years old, and 68% of the patients had a BMI of less than 25. Gender, IVDA, HAART, BMI, and age were not associated as risk factors for the prevalence of DM in the studied population. DISCUSSION: Our data revealed a higher prevalence of DM in HIV infected patients. We observed no significant association between DM and its risks factors. This raises concern for yet unrecognized risk factors contributing to a higher prevalence of the disease in this population. Results of our study alert physicians on the importance of DM screening in the HIV positive patient population.


OBJECTIVES: To determine the lung cancer incidence and survival time among HIV-infected and uninfected women and men. DESIGN: Two longitudinal studies of HIV infection in the United States. METHODS: Data from 2549 women in the Women's Interagency HIV Study (WIHS) and 4274 men in the Multicenter AIDS Cohort Study (MACS), all with a history of cigarette smoking, were analyzed. Lung cancer incidence rates and incidence rate ratios were calculated using Poisson regression analyses. Survival time was assessed using Kaplan-Meier and Cox proportional-hazard analyses. RESULTS: Thirty-seven women and 23 men developed lung cancer (46 HIV-infected and 14 HIV-uninfected) during study follow-up. In multivariable analyses, the factors that were found to be independently associated with a higher lung cancer incidence rate ratios were older age, less education, 10 or more pack-years of smoking, and a prior diagnosis of AIDS pneumonia (vs. HIV-uninfected women). In an adjusted Cox model that allowed different hazard functions for each cohort, a history of injection drug use was associated with shorter survival, and a lung cancer diagnosis after 2001 was associated with longer survival. In an adjusted Cox model restricted to HIV-infected participants, nadir CD4 lymphocyte cell count less than 200 was associated with shorter survival time. CONCLUSIONS: Our data suggest that pulmonary damage and inflammation associated with HIV infection may be causative for the increased risk of lung cancer. Encouraging and assisting younger HIV-infected smokers to quit and to sustain cessation of smoking is imperative to reduce the lung cancer burden in this population.

To characterize the relationship between dispersion-based intra-individual variability (IIVd) in neuropsychological test performance and brain volume among HIV seropositive and seronegative men and to determine the effects of cardiovascular risk and HIV infection on this relationship. Magnetic Resonance Imaging (MRI) was used to acquire high-resolution neuroanatomic data from 147 men age 50 and over, including 80 HIV seropositive (HIV+) and 67 seronegative controls (HIV-) in this cross-sectional cohort study. Voxel Based Morphometry was used to derive volumetric measurements at the level of the individual voxel. These brain structure maps were analyzed using Statistical Parametric Mapping (SPM2). IIVd was measured by computing intra-individual standard deviations (ISD's) from the standardized performance scores of five neuropsychological tests: Wechsler Memory Scale-III Visual Reproduction I and II, Logical Memory I and II, Wechsler Adult Intelligence Scale-III Letter Number Sequencing. Total gray matter (GM) volume was inversely associated with IIVd. Among all subjects, IIVd-related GM atrophy was observed primarily in: 1) the inferior frontal gyrus bilaterally, the left inferior temporal gyrus extending to the supramarginal gyrus, spanning the lateral sulcus; 2) the right superior parietal lobule and intraparietal sulcus; and, 3) dorsal/ventral regions of the posterior section of the transverse temporal gyrus. HIV status, biological, and cardiovascular disease (CVD) variables were not linked to IIVd-related GM atrophy. IIVd in neuropsychological test performance may be a sensitive marker of cortical integrity in older adults, regardless of HIV infection status or CVD risk factors, and degree of intra-individual variability links with volume loss in specific cortical regions; independent of mean-level performance on neuropsychological tests.


Although the decline in cancer mortality rates with the advent of combination antiretroviral therapy (cART) in HIV-infected individuals can be mostly explained by a decrease in cancers incidence, we looked here if improved survival after cancer diagnosis could also contribute to this decline. Survival trends were analyzed for most frequent cancers in the HIV-infected population followed in the French Hospital Database on HIV: 979 and 2,760 cases of visceral and non-visceral Kaposi's sarcoma (KS), 2,339 and 461 cases of non-Hodgkin lymphoma (NHL) and Hodgkin's lymphoma (HL), 446 lung, 312 liver and 257 anal cancers. Five-year Kaplan-Meier survival rates were estimated for four periods: 1992-1996, 1997-2000, 2001-2004 and 2005-2009. Cox proportional hazard models were used to compare survival across the periods, after adjustment for confounding factors. For 2001-2004, survival was compared to the general population after standardization on age and sex. Between the pre-cART (1992-1996) and early-cART (1997-2000) periods, survival improved after KS, NHL, HL and anal cancer and remained stable after lung and liver cancers. During the cART era, 5-year survival improved after visceral and non-visceral KS, NHL, HL and liver cancer, being 83, 92, 65, 87 and 19% in 2005-2009, respectively, and remained stable after lung and anal cancers, being 16 and 65%, respectively. Compared with the general population, survival in HIV-infected individuals in 2001-2004 was poorer for hematological malignancies and similar for solid tumors. For hematological malignancies, survival continues to improve after 2004, suggesting that the gap between the HIV-infected and general populations will close in the future.


BACKGROUND: Clinical care for older adults is complex and represents a growing problem. They are a diverse patient group with varying needs, frequent presence of multiple comorbidities, and are more susceptible to treatment harms. Thus Clinical Practice Guidelines (CPGs) need to carefully consider older adults in order to guide clinicians. We reviewed CPG recommendations for primary cardiovascular disease (CVD) prevention and examined the extent to which CPGs address issues important for older people identified in the literature. METHODS: We
searched: 1) two systematic reviews on CPGs for CVD prevention and 2) the National CPG Clearinghouse, G-I-N International CPG Library and Trip databases for CPGs for CVD prevention, hypertension and cholesterol. We conducted our search between April and December 2013. We excluded CPGs for diabetes, chronic kidney disease, HIV, lifestyle, general screening/prevention, and pregnant or pediatric populations. Three authors independently screened citations for inclusion and extracted data. The primary outcomes were presence and extent of recommendations for older people including discussion of: (1) available evidence, (2) barriers to implementation of the CPG, and (3) tailoring management for this group. RESULTS: We found 47 eligible CPGs. There was no mention of older people in 4 (9 %) of the CPGs. Benefits were discussed more frequently than harms. Twenty-three CPGs (49 %) discussed evidence about potential benefits and 18 (38 %) discussed potential harms of CVD prevention in older people. Most CPGs addressed one or more barriers to implementation, often as a short statement. Although 27 CPGs (58 %) mentioned tailoring management to the older patient context (e.g. comorbidities), concrete guidance was rare. CONCLUSION: Although most CVD prevention CPGs mention the older population to some extent, the information provided is vague and very limited. Older adults represent a growing proportion of the population. Guideline developers must ensure they consider older patients’ needs and provide appropriate advice to clinicians in order to support high quality care for this group. CPGs should at a minimum address the available evidence about CVD prevention for older people, and acknowledge the importance of patient involvement.


Chronic pain is common in HIV, but incompletely characterized, including its underlying etiologies, its effect on healthcare utilization, and the characteristics of affected patients in the HIV primary care setting. These data are needed in order to design and justify appropriate clinic-based pain management services. Using a clinical data warehouse, we analyzed one year of data from 638 patients receiving standard-of-care antiretroviral therapy in a large primary care HIV clinic, located in the Harlem neighborhood of New York City. We found that 40% of patients carried one or more chronic pain diagnoses. The most common diagnoses were degenerative musculoskeletal disorders (e.g. degenerative spinal disease and osteoarthritis), followed by neuropathic pain and headache disorders. Many patients (16%) had multiple chronic pain diagnoses. Women, older patients, and patients with greater burdens of medical illness, and psychiatric and substance use co-morbidities were disproportionately represented among those with chronic pain diagnoses. Controlling for overall health status, HIV patients with chronic pain had greater healthcare utilization including emergency department visits and radiology procedures. In summary, our study demonstrates the high prevalence of chronic pain disorders in the primary care HIV clinic. Co-located interventions for chronic pain in this setting should focus on musculoskeletal pain but also account for complex multifaceted pain syndromes, and address the unique biopsychosocial features of this population. Furthermore since chronic pain is prevalent in HIV and associated with increased healthcare utilization, developing clinic-based pain management programs could be cost-effective.


BACKGROUND: The burden of non-communicable diseases (NCDs) is increasing in sub-Saharan Africa, but data available for intervention planning are inadequate. We determined the prevalence of selected NCDs and HIV infection, and NCD risk factors in northwestern Tanzania and southern Uganda. METHODS: A population-based cross-sectional survey was conducted, enrolling households using multistage sampling with five strata per country (one municipality, two towns, two rural areas). Consenting adults (> /= 18 years) were interviewed using the WHO STEPS
survey instrument, examined, and tested for HIV and diabetes mellitus (DM). Adjusting for survey design, we estimated population prevalences of hypertension, DM, obstructive pulmonary disease, cardiac failure, epilepsy and HIV, and investigated factors associated with hypertension using logistic regression. RESULTS: Across strata, hypertension prevalence ranged from 16 % (95 % confidence interval (CI): 12 % to 22 %) to 17 % (CI: 14 % to 22 %) in Tanzania, and from 19 % (CI: 14 % to 26 %) to 26 % (CI: 23 % to 30 %) in Uganda. It was high in both urban and rural areas, affecting many young participants. The prevalence of DM (1 % to 4 %) and other NCDs was generally low. HIV prevalence ranged from 6 % to 10 % in Tanzania, and 6 % to 12 % in Uganda. Current smoking was reported by 12 % to 23 % of men in different strata, and 1 % to 3 % of women. Problem drinking (defined by Alcohol Use Disorder Identification Test criteria) affected 6 % to 15 % men and 1 % to 6 % women. Up to 46 % of participants were overweight, affecting women more than men and urban more than rural areas. Most patients with hypertension and other NCDs were unaware of their condition, and hypertension in treated patients was mostly uncontrolled. Hypertension was associated with older age, male sex, being divorced/widowed, lower education, higher BMI and, inversely, with smoking. CONCLUSIONS: The high prevalence of NCD risk factors and unrecognized and untreated hypertension represent major problems. The low prevalence of DM and other preventable NCDs provides an opportunity for prevention. HIV prevalence was in line with national data. In Tanzania, Uganda and probably elsewhere in Africa, major efforts are needed to strengthen health services for the PREVENTION, early detection and treatment of chronic diseases.


OBJECTIVES: In HIV-uninfected populations, obstructive sleep apnoea (OSA) is commonly associated with cardiovascular disease, metabolic syndrome, and cognitive impairment. These comorbidities are common in HIV-infected patients, but there are scarce data regarding OSA in HIV-infected patients. Therefore, we examined the prevalence and correlates of OSA in a cohort of HIV-infected and uninfected patients. METHODS: An observational cohort study was carried out. Electronic medical record and self-report data were examined in patients enrolled in the Veterans Aging Cohort Study (VACS) between 2002 and 2008 and followed until 2010. The primary outcome was OSA diagnosis, determined using International Classification of Diseases, 9th edition (ICD-9) codes, in HIV-infected compared with uninfected individuals. We used regression analyses to determine the association between OSA diagnosis, symptoms and comorbidities in adjusted models. RESULTS: Of 3683 HIV-infected and 3641 uninfected patients, 143 (3.9%) and 453 (12.4%) had a diagnosis of OSA (p<0.0001), respectively. HIV-infected patients were more likely to report symptoms associated with OSA such as tiredness and fatigue. Compared with uninfected patients with OSA, HIV-infected patients with OSA were younger, had lower body mass indexes (BMIs), and were less likely to have hypertension. In models adjusting for these traditional OSA risk factors, HIV infection was associated with markedly reduced odds of OSA diagnosis (odds ratio 0.48; 95% confidence interval 0.39-0.60). CONCLUSIONS: HIV-infected patients are less likely to receive a diagnosis of OSA. Future studies are needed to determine whether the lower prevalence of OSA diagnoses in HIV-infected patients is attributable to decreased screening and detection or to a truly decreased likelihood of OSA in the setting of HIV infection.

BACKGROUND: HIV-infected persons are at increased cardiovascular disease (CVD) risk, but traditional CVD therapies are understudied in this population. Telmisartan is an angiotensin receptor blocker (ARB) and peroxisome proliferator-activated receptor-gamma (PPAR-gamma) agonist that improves endothelial function and cardiovascular mortality in HIV-uninfected populations. We assessed the effects of telmisartan on endothelial function in older HIV-infected persons at risk for CVD in a small pilot study. METHODS: HIV-infected individuals >/=50 years old on suppressive antiretroviral therapy (ART) with >/=1 traditional CVD risk factor received open-label telmisartan 80 mg daily for 6 weeks. Brachial artery flow-mediated dilation (FMD) measured endothelial function. The primary endpoint was 6-week change in maximum relative FMD. RESULTS: Seventeen participants enrolled; 16 completed all evaluations (88% men, 65% non-White, median age 60 years, CD4+T lymphocyte count 625 cells/mm3). Antiretroviral therapy included 71% protease inhibitor (PI), 29% non-nucleoside reverse transcriptase inhibitor (NNRTI), 29% integrase inhibitor, 65% tenofovir, and 29% abacavir. Cardiovascular disease risk factor prevalence included 76% hyperlipidemia, 65% hypertension, 18% smoking, and 12% diabetes mellitus. After 6 weeks, statistically significant blood pressure changes were observed (systolic -16.0 mmHg, diastolic -6.0 mmHg) without significant changes in FMD. In subset analyses, FMD increased more among abacavir-treated, PI-treated, and non-smoking participants. CONCLUSIONS: No significant FMD changes were observed after 6 weeks of telmisartan therapy; however, abacavir- and PI-treated participants and non-smokers showed greater FMD increases. Additional studies are needed to explore the effects of telmisartan on endothelial function among HIV-infected individuals with traditional CVD and/or ART-specific risk factors.


We describe four cases of hand osteoarthritis in patients with HIV infection under antiretroviral treatment. A 36-year-old HIV-infected man came for consultation in 2007 with hand osteoarthritis. He was diagnosed HIV positive by sexual transmission in 1997. A 52-year-old HIV-infected woman came for consultation with hand osteoarthritis started in 2006. She was diagnosed HIV positive in 1986 by sexual transmission. A 57-year-old man presented hand osteoarthritis. This former IV drug user was diagnosed HIV positive in 1989. A 61-year-old HIV-infected man presented with hand osteoarthritis started in 2010. He had been contaminated with HIV in 1990 by sexual transmission. For all patients, there were neither clinical nor biological manifestations suggesting inflammatory arthritis. X-rays showed signs of hand osteoarthritis. CD4 cell count was over 500/mm(3) and the viral load was below 20 copies/mL under treatments. These four cases show osteoarthritis in HIV-infected patients. Hand osteoarthritis did not seem to be linked to aging or to an antiretroviral treatment's side effect, but rather to the HIV infection itself, and it may pass through a metabolic syndrome. We described a possible association between early-developed hand osteoarthritis and HIV-infected patients. Clinicians should consider osteoarthritis when they are confronted with HIV-infected patients with chronic hand pain.

intravenous drug abuse or hepatitis C infection) (n = 3205), and a background population cohort matched by age, gender, and country of birth (n = 22 435) were analyzed. Educational level (low or high) and cancer events were identified in Danish national registers. Cumulative incidences, incidence rate ratios (IRRs), and survival using Kaplan-Meier methods were estimated. RESULTS: Low educational level was associated with increased risk of cancer among HIV-infected individuals compared to population controls: all (adjusted-IRRs: 1.4 [95% confidence interval {CI}, 1.1-1.7] vs 1.1 [95% CI, .9-1.2]), tobacco- and alcohol-related (2.1 [95% CI, 1.3-3.4] vs 1.3 [95% CI, 1.1-1.6]), and other (1.7 [95% CI, 1.1-2.8] vs 0.9 [95% CI, .7-1.0]). Educational level was not associated with infection-related or ill-defined cancers. One-year-survival was not associated with educational level, but HIV-infected individuals with low educational level had lower 5-year-survival following infection-related and ill-defined cancers. CONCLUSIONS: Education is associated with risk and prognosis of some cancers in HIV infection, and diverges from what is observed in the background population.


INTRODUCTION: Both natural history and epidemiological trend of HIV infection have been deeply modified by the introduction of highly active antiretroviral therapy (HAART), around twenty years ago. METHODS: However, despite a rapid drop of the incidence of the large majority of opportunistic infections, a slow, but continued increase of malignancies occurred, with particular evidence focused on cancers which are not strictly related to the definition of full blown AIDS (the so called non-AIDS-defining malignancies). RESULTS: The unique clinical occurrence of HIV infection complicated by even four non-AIDS-defining cancers prompted us to re-discuss the epidemiology and the possible pathogenesis, the clinical presentation, and the differential diagnosis of this pathologic presentation. CONCLUSIONS: On the ground of our experience in this field, and the available literature evidences, we discuss how this clinical occurrence is acting on HIV infection presentation during the HAART era of the third millennium. These changes need broad scale studies, and promise relevant consequences on etiopathogenetic, prevention, therapeutic, and management aspects of HIV disease in the next future.


Claims of accelerated or premature aging are frequently made. However, the lack of standard criteria for measuring speed of aging makes such claims highly questionable. Because of fundamental gaps in our current understanding of the biological mechanisms of aging, the development of specific phenotypes that are due to aging is difficult and such phenotypes can only be derived by observational data. However, a clinical phenotype of aging exists that is experienced by all living individuals and is pervasive across multiple physiologic systems. Characterizing this phenotype can serve as a basis for measuring the speed of aging, and can facilitate a better understanding of the aging process and its interaction with chronic diseases.

With more effective and widespread antiretroviral treatment, the overall incidence of AIDS- or HIV-related death has decreased dramatically. Consequently, as patients are aging, cardiovascular disease (CVD) has emerged as an important cause of morbidity and mortality in the HIV population. The incidence of CVD overall in HIV is relatively low, but it is approximately 1.5-2-fold higher than that seen in age-matched HIV-uninfected individuals. Multiple factors are believed to explain this excess in risk such as overrepresentation of traditional cardiovascular risk factors (particularly smoking), toxicities associated with cumulative exposure to some antiretroviral agents, together with persistent chronic inflammation, and immune activation associated with HIV infection. Tools are available to calculate an individual's predicted risk of CVD and should be incorporated in the regular follow-up of HIV-infected patients. Targeted interventions to reduce this risk must be recommended, including life-style changes and medical interventions that might include changes in antiretroviral therapy.


OBJECTIVE: Positive remodeling (PR), a coronary artery characteristic associated with risk for myocardial infarction (MI), may be more prevalent in HIV-infected (HIV+) people. We evaluated the prevalence of PR using coronary CT angiography (CCTA) in HIV+ and HIV-uninfected (HIV-) men. METHODS: Men enrolled in the Multicenter AIDS Cohort Study underwent CCTA if they were 40-70 years, had normal kidney function and no history of coronary revascularization. Multivariable logistic regression models were used to estimate the odds ratio (OR) of PR by HIV serostatus, adjusting for demographics and coronary artery disease (CAD) risk factors. Analysis of PR among atherosclerotic segments further adjusted for plaque type and stenosis. RESULTS: The prevalence of PR was 8.4% versus 12.1% (p = 0.10) for HIV- and HIV + men, respectively. After demographic adjustment, HIV + men had twice the odds of PR [OR 2.01(95% CI 1.20 3.38)], which persisted after CAD risk factor adjustment [1.76(1.00-3.10)]. Higher systolic blood pressure, total cholesterol, diabetes medication use, older age, segment number with plaque present, mixed and non-calcified plaque, and stenosis>50%, were associated with increased odds of PR, while higher HDL cholesterol, higher nadir CD4 count, and black race were associated with lower PR odds. Among atherosclerotic segments, the association between HIV infection and PR persisted, but was not statistically significantly. CONCLUSION: HIV+ men have more positively remodeled arterial segments, which may be due to more coronary segments with atherosclerosis or HIV-related immunosuppression. Further studies are needed to evaluate whether PR contributes to higher rates of MI in HIV+ individuals.


BACKGROUND: As persons with HIV live longer, data regarding the epidemiology of colorectal cancer are required to optimize the long-term management of these patients. The purpose of this systematic review and meta-analysis is to synthesize evidence regarding the incidence of colorectal cancer in persons with HIV. METHODS/DESIGN: Our primary outcome is the standardized incidence ratio of colorectal cancer among persons with HIV relative to rates in persons not living with HIV. Our secondary objectives are to summarize the evidence for differences with respect to stage at diagnosis, site of disease, and mortality due to colorectal cancer. We will search electronic bibliographic databases from their inception date, as well as conference proceedings and reference lists of included articles. Two investigators will independently screen citations and full-text articles, conduct data abstraction, and appraise study quality. We will examine clinical, methodological, and statistical heterogeneity among studies prior to conducting meta-analysis. Random effects meta-analysis methods will be employed to estimate standardized incidence ratios. These data will inform the development of guidelines for colorectal cancer screening in persons with HIV.

SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42014013449.

BACKGROUND: Anal cancer is a priority health issue in HIV positive men who have sex with men. Anal cancer screening may be aimed at either detecting the precursor lesion (high grade anal intraepithelial neoplasia[HGAIN]) or early anal cancer. To date no qualitative study has explored the views of HIV physicians regarding anal cancer and its screening. METHODS: We conducted indepth interviews with 20 HIV physicians (Infectious diseases, Immunology, Sexual health, General practice) in different settings (hospital, sexual health centres, general practice) from around Australia. Framework analysis was used to identify themes. RESULTS: HIV physicians viewed anal cancer as a significant health issue and all agreed on the importance of anal cancer screening amongst HIV positive MSM if a valid screening method was available. Barriers for utilizing anal cytology was based primarily on the theme of insufficient evidence (e.g. no studies demonstrating reduction in mortality following screening or effective treatments for HGAIN). Barriers for utilizing DARE for early cancer detection were based on systemic factors (e.g. lack of opportunity, lack of priority, differences in HIV care practices); health provider factors (lack of evidence, difficulty discussing with patients, lack of confidence in DARE) and patient factors (perceived discomfort of DARE for patients, low anal cancer risk awareness). Physicians were willing to consider the idea of patient self-examination and partner-examination although concerns were raised regarding its reliability and issues surrounding partner dynamics. CONCLUSIONS: HIV physicians remain ambivalent regarding the most effective means to screen for anal cancer. More research is needed to address the physicians’ concerns before anal cancer screening can be implemented into routine HIV care.


BACKGROUND: Combination antiretroviral therapy (cART) had a dramatic impact on the mortality profile in human immunodeficiency virus (HIV) infected individuals and increased their life-expectancy. Conditions associated with the aging process have been diagnosed more frequently among HIV-infected patients, particularly, cardiovascular diseases. METHODS: Patients followed in the Instituto de Pesquisa Clinica Evandro Chagas (IPEC) prospective cohort in Rio de Janeiro were submitted to the general procedures from the Brazilian Longitudinal Study of Adult Health, comprising several anthropometric, laboratory and imaging data. Carotid intima-media thickness (cIMT) was measured by ultrasonography, following the Mannheim protocol. Linear regression and proportional odds models were used to compare groups and covariables in respect to cIMT. The best model was chosen with the adaptive lasso procedure. RESULTS: A valid cIMT exam was available for 591 patients. Median cIMT was significantly larger for men than women (0.56mm vs. 0.53mm; p = 0.002; overall = 0.54mm). In univariable linear regression analysis, both traditional risk factors for cardiovascular diseases (CVD) and HIV-specific characteristics were significantly associated with cIMT values, but the best multivariable model chosen included only traditional characteristics. Hypertension presented the strongest association with higher cIMT terciles (OR = 2.51; 95%CI = 1.69-3.73), followed by current smoking (OR = 1.82; 95%CI = 1.19-2.79), family history of acute myocardial infarction or stroke (OR = 1.60; 95%CI = 1.10-2.32) and age (OR per year = 1.12; 95%CI = 1.10-1.14). CONCLUSIONS: Our results show that traditional cardiovascular disease (CVD) risk factors are the major players in determining increased cIMT among HIV infected patients in Brazil. This finding reinforces the need for thorough assessment of those risk factors in these patients to guarantee the incidence of CVD events remain under control.

BACKGROUND: The number of HIV-positive people aged ≥50 years is rising each year. We measured the prevalence of non-infectious illnesses and their risk factors and described healthcare use in this UK population.

METHODS: A cross-sectional, observational study conducted at an outpatient HIV specialist clinic in south east England. Patients age ≥50 years were invited to complete questionnaires measuring demographics, non-infectious illnesses, medication use, lifestyle and healthcare utilisation.

RESULTS: The response rate was 67%. Of 299 participants, 84% reported ≥1 comorbid condition and 61% reported ≥2 (multimorbidity). Most commonly reported were high cholesterol, sexual dysfunction, hypertension and depression. In multivariate analyses, age, number of years HIV positive and duration of antiretroviral therapy remained significant predictors of comorbidity when controlling for lifestyle factors (exercise, smoking and use of recreational drugs and alcohol). Use of non-HIV healthcare services was associated with increasing comorbidity, a longer duration of HIV and recreational drug use.

CONCLUSIONS: The majority of HIV-patients aged ≥50 years reported multiple comorbidities and this was associated with polypharmacy and increased use of non-HIV services. Further research examining the quality, safety and patient experience of healthcare is needed to inform development of services to optimally meet the needs of older HIV-positive patients.


BACKGROUND: Self-reported quality of life (QoL) has previously been found to be impaired in patients living with HIV and associated with viral replication, degree of immunodeficiency, and comorbidity. We aimed at investigating QoL in a group of HIV-infected patients with suppressed viral replication and with low comorbidity, compared with healthy controls. We furthermore aimed to identify factors associated with QoL.

METHODS: Cross-sectional study of 52 HIV-infected patients and 23 healthy controls matched on age, gender, education, and comorbidity. HIV-infected patients and healthy controls had previously been examined regarding cognitive, physical, metabolic, and immunological parameters. QoL was investigated using the Medical Outcomes Study HIV Health Survey (MOS-HIV). Linear multiple regression models were created to find factors associated with mental health summary score (MHS) and physical health summary score (PHS).

RESULTS: HIV-infected patients reported lower QoL compared with controls. In HIV-infected patients, female gender and depression score were associated with lower MHS. In controls, years of education, depression score, and cognitive test performance were associated with lower MHS. In HIV-infected patients, years of education, depression score, and body mass index were associated with lower PHS, whereas in controls, years of education and fitness level were associated with PHS.

CONCLUSIONS: Even well-treated HIV-infected patients with low level of comorbidity reported lower QoL compared with healthy controls. Especially, depression score and body mass index were associated with QoL in HIV-infected patients.


This article provides an overview of the current literature on seven cancer sites that may disproportionately affect lesbian, gay, bisexual, transgender/transsexual, and queer/questioning (LGBTQ) populations. For each cancer site, the authors present and discuss the descriptive statistics, primary prevention, secondary prevention and preclinical disease, tertiary prevention and late-stage disease, and clinical implications. Finally, an overview of psychosocial factors related to cancer survivorship is offered as well as strategies for improving access to care.
Rates of abnormal visual inspection with acetic acid and prevalence of high-risk human papillomavirus (HPV) subtypes have not been well characterized in HIV-infected women in Malawi. We performed a prospective cohort study of visual inspection with acetic acid (N = 440) in HIV-infected women aged 25–59 years, with a nested study of HPV subtypes in first 300 women enrolled. Of 440 women screened, 9.5% (N = 42) had abnormal visual inspection with acetic acid with 69.0% (N = 29) having advanced disease not amenable to cryotherapy. Of 294 women with HPV results, 39% (N = 114) of women were positive for high-risk HPV infection. Only lower CD4 count (287 cells/mm\(^3\) versus 339 cells/mm\(^3\), p = 0.03) and high-risk HPV (66.7% versus 35.6%, p < 0.01) were associated with abnormal visual inspection with acetic acid. The most common high-risk HPV subtypes in women with abnormal visual inspection with acetic acid were 35 (33.3%), 16 (26.7%), and 58 (23.3%). Low CD4 cell count was associated with abnormal visual inspection with acetic acid and raises the importance of early antiretroviral therapy and expanded availability of visual inspection with acetic acid. HPV vaccines targeting additional non-16/18 high-risk HPV subtypes may have greater protective advantages in countries such as Malawi.

We surveyed trends in incidence (1995-2012) and risk factors for anal cancer in the Dutch HIV-positive population. After an initial increase with a peak incidence in 2005-2006 of 114 [95% confidence interval (CI): 74 to 169] in all HIV+ patients and 168 (95% CI: 103 to 259) in HIV+ men who have sex with men (MSM), a decline to 72 (95% CI: 43 to 113) and 100 (95% CI: 56 to 164), respectively, was seen in 2011-2012. Low nadir CD4, alcohol use, and smoking were significantly associated with anal cancer in MSM. In conclusion, anal cancer remains a serious problem in predominantly HIV+ MSM. However, it seems that incidence rates are leveling off.

The rise in prevalence of chronic diseases has become a global healthcare priority and a system wide approach has been called for to manage this growing epidemic. Whilst healthcare reform to tackle the scale of chronic disease and other long term conditions is still in its infancy, there is an emerging recognition that in an ageing society, people often suffer from more than one chronic disease at the same time. Multimorbidity poses new and distinct challenges and was the focus of a global conference held by the Organization of Economic Cooperation and Development (OECD) in 2011. Health education was raised as requiring radical redesign to equip graduates with the appropriate skills to face the challenges ahead. We wanted to explore how different aspects of multimorbidity were addressed within pre-registration nurse education and held an international (United Kingdom-Sweden) nurse workshop in Linkoping, Sweden in April 2013, which included nurse academics and clinicians. We also sent questionnaire surveys to final year student nurses from both countries. This paper explores the issues of multimorbidity from a patient, healthcare and nurse education perspective and presents the preliminary discussions from the workshop and students' survey.
OBJECTIVES: We used population-based data to identify incident cancer cases and correlates of cancer among women living with HIV/AIDS in British Columbia (BC), Canada between 1994 and 2008. METHODS: Data were obtained from a retrospective population-based cohort created from linkage of two province-wide databases: (1) the database of the BC Cancer Agency, a province-wide population-based cancer registry, and (2) a database managed by the BC Centre for Excellence in HIV/AIDS, which contains data on all persons treated with antiretroviral therapy in BC. This analysis included women (>/= 19 years old) living with HIV in BC, Canada. Incident cancer diagnoses that occurred after highly active antiretroviral therapy (HAART) initiation were included. We obtained a general population comparison of cancer incidence among women from the BC Cancer Agency. Bivariate analysis (Pearson chi2 , Fisher's exact or Wilcoxon rank-sum test) compared women with and without incident cancer across relevant clinical and sociodemographic variables. Standardized incidence ratios (SIRs) were calculated for selected cancers compared with the general population sample. RESULTS: We identified 2211 women with 12 529 person-years (PY) of follow-up who were at risk of developing cancer after HAART initiation. A total of 77 incident cancers (615/100 000 PY) were identified between 1994 and 2008. HIV-positive women with cancer, in comparison to the general population sample, were more likely to be diagnosed with invasive cervical cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma and Kaposi's sarcoma and less likely to be diagnosed with cancers of the digestive system. CONCLUSIONS: This study observed elevated rates of cancer among HIV-positive women compared to a general population sample. HIV-positive women may have an increased risk for cancers of viral-related pathogenesis.


Both HIV disease and advanced age have been associated with alterations to cerebral white matter, as measured with white matter hyperintensities (WMH) on fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI), and more recently with diffusion tensor imaging (DTI). This study investigates the combined effects of age and HIV serostatus on WMH and DTI measures, as well as the relationships between these white matter measures, in 88 HIV seropositive (HIV+) and 49 seronegative (HIV-) individuals aged 23-79 years. A whole-brain volumetric measure of WMH was quantified from FLAIR images using a semi-automated process, while fractional anisotropy (FA) was calculated for 15 regions of a whole-brain white matter skeleton generated using tract-based spatial statistics (TBSS). An age by HIV interaction was found indicating a significant association between WMH and older age in HIV+ participants only. Similarly, significant age by HIV interactions were found indicating stronger associations between older age and decreased FA in the posterior limbs of the internal capsules, cerebral peduncles, and anterior corona radiata in HIV+ vs. HIV- participants. The interactive effects of HIV and age were stronger with respect to whole-brain WMH than for any of the FA measures. Among HIV+ participants, greater WMH and lower anterior corona radiata FA were associated with active hepatitis C virus infection, a history of AIDS, and higher current CD4 cell count. Results indicate that age exacerbates HIV-associated abnormalities of whole-brain WMH and fronto-subcortical white matter integrity.


BACKGROUND: We previously reported that fracture incidence rates did not differ by HIV status among predominantly premenopausal Women's Interagency HIV Study participants. We now conduct a follow-up study with 5 additional observation years to further characterize fracture risk associated with HIV infection in women as they age. METHODS: We measured time to first new fracture at any site in 2375 (1713 HIV-infected and 662 HIV-uninfected) Women's Interagency HIV Study participants, with median 10-year follow-up. Fractures were self-reported semiannually. Proportional hazards models assessed predictors of incident fracture. RESULTS: At index visit, HIV-infected women were older [median age of 40 years (IQR: 34-46) vs. 35 (27-43), P < 0.0001] and more likely to be
postmenopausal, hepatitis C virus infected, and weigh less than HIV-uninfected women. Among HIV-infected women, mean CD4 count was 480 cells per microliter and 63% were taking highly active antiretroviral therapy. Unadjusted incidence rates of any fracture were higher in HIV-infected than in HIV-uninfected women [2.19/100 person-years (py) vs. 1.54/100 py, \( P = 0.002 \)]. In multivariate models, HIV status, older age, white (vs. black) race, prior fracture, history of cocaine use, and history of injection drug use were significant predictors of incident fracture. Among HIV-infected women, age, white race, prior fracture, smoking, and prior AIDS were predictors of new fracture.

CONCLUSIONS: Middle-aged HIV-infected women had a higher adjusted fracture rate than HIV-uninfected women. Cocaine use and injection drug use were also associated with a greater risk of incident fracture. Further research is needed to understand whether the risk of fracture associated with cocaine use relates to increased rate of falls or direct effects on bone metabolism.


BACKGROUND: Cancer is increasingly common among persons with HIV. OBJECTIVE: To examine calendar trends in cumulative cancer incidence and hazard rate by HIV status. DESIGN: Cohort study. SETTING: North American AIDS Cohort Collaboration on Research and Design during 1996 to 2009. PARTICIPANTS: 86 620 persons with HIV and 196 987 uninfected adults. MEASUREMENTS: Cancer type-specific cumulative incidence by age 75 years and calendar trends in cumulative incidence and hazard rates, each by HIV status. RESULTS: Cumulative incidences of cancer by age 75 years for persons with and without HIV, respectively, were as follows: Kaposi sarcoma, 4.4% and 0.01%; non-Hodgkin lymphoma, 4.5% and 0.7%; lung cancer, 3.4% and 2.8%; anal cancer, 1.5% and 0.05%; colorectal cancer, 1.0% and 1.5%; liver cancer, 1.1% and 0.4%; Hodgkin lymphoma, 0.9% and 0.09%; melanoma, 0.5% and 0.6%; and oral cavity/pharyngeal cancer, 0.8% and 0.8%. Among persons with HIV, calendar trends in cumulative incidence and hazard rate decreased for Kaposi sarcoma and non-Hodgkin lymphoma. For anal, colorectal, and liver cancer, increasing cumulative incidence, but not hazard rate trends, were due to the decreasing mortality rate trend (-9% per year), allowing greater opportunity to be diagnosed. Despite decreasing hazard rate trends for lung cancer, Hodgkin lymphoma, and melanoma, cumulative incidence trends were not seen because of the compensating effect of the declining mortality rate. LIMITATION: Secular trends in screening, smoking, and viral co-infections were not evaluated. CONCLUSION: Cumulative cancer incidence by age 75 years, approximating lifetime risk in persons with HIV, may have clinical utility in this population. The high cumulative incidences by age 75 years for Kaposi sarcoma, non-Hodgkin lymphoma, and lung cancer support early and sustained antiretroviral therapy and smoking cessation.


BACKGROUND: To effectively meet the health care needs of multimorbid patients, the most important psychosocial factors associated with multimorbidity must be discerned. Our aim was to examine the association between self-reported adverse childhood experiences (ACEs) and multimorbidity and the contribution of other social, behavioural and psychological factors to this relationship. METHODS: We analysed cross-sectional data from the Mitchelstown study, a population-based cohort recruited from a large primary care centre. ACE was measured by self-report using the Centre for Disease Control ACE questionnaire. Multimorbidity status was categorized as 0, 1 or \( >1 \) chronic diseases, which were ascertained by self-report of doctor diagnosis. Ordinal logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) for multimorbidity, using ACE as the independent variable with adjustment for social (education, public health cover), behavioural (smoking, exercise, diet, body mass index) and psychological factors (anxiety/depression scores). RESULTS: Of 2047 participants, 45.3% (n = 927, 95% CI: 43.1-47.4) reported multimorbidity. ACE was reported by 28.4% (n = 248, 95% CI: 25.3-31.3%) of multimorbid
participants, 21% (n = 113, 95% CI: 18.0-25.1%) of single chronic disease participants and 16% (n = 83, 95% CI: 13.2-19.7%) of those without chronic disease. The OR for multimorbidity with any history of ACE was 1.6 (95% CI: 1.4-2.0, P < 0.001). Adjusting for social, behavioural and psychological factors only marginally ameliorated this association, OR 1.4 (95% CI: 1.1-1.7, P = 0.002). CONCLUSIONS: Multimorbidity is independently associated with a history of ACEs. These findings demonstrate the psychosocial complexity associated with multimorbidity and should be used to inform health care provision in this patient cohort.


Modern medical management of comorbid conditions has resulted in escalating use of multiple medications and the emergence of the twin phenomena of multimorbidity and polypharmacy. Current understanding of how the polypharmacy in conjunction with multimorbidity influences trauma outcomes is limited, although it is known that trauma patients are at increased risk for medication-related adverse events. The comorbidity-polypharmacy score (CPS) is a simple clinical tool that quantifies the overall severity of comorbidities using the polypharmacy as a surrogate for the "intensity" of treatment necessary to adequately control chronic medical conditions. Easy to calculate, CPS is derived by counting all known pre-injury comorbid conditions and medications. CPS has been independently associated with mortality, increased risk for complications, lower functional outcomes, readmissions, and longer hospital stays. In addition, CPS may help identify older trauma patients at risk of post-emergency department undertriage. The goal of this article was to review and refine the rationale for CPS and to provide an evidence-based outline of its potential clinical applications.


Aging is associated with an increase in a chronic, low-grade inflammation. This phenomenon, termed "inflammaging" is also a risk factor for both morbidity and mortality in the elderly. Frequent co-occurrence of chronic diseases, known as multi-morbidity, may be explained by interconnected pathophysiology of these conditions, most of which depend on its inflammatory component. Here we present an analysis of the U.S. National Health and Nutrition Examination Survey data collected between 1999 and 2008, for the presence, and the number, of chronic diseases along with HDL-cholesterol, C-reactive protein, white blood cell count, lymphocyte percent, monocyte percent, segmented neutrophils percent, eosinophils percent, basophils percent, and glycohemoglobin levels. Importantly, even after adjustment for age and BMI, many inflammatory markers continued to be associated to multi-morbidity. C-reactive protein (CRP) levels and Glasgow Prognostic Score (GPS) were most dramatically increased in parallel with an accumulation of chronic diseases, and may be utilized as multi-morbidity predictors. These observations point at background inflammation as direct, age-independent contributor to an accumulation of the disease burden. Our findings also suggest a possibility that systemic inflammation associated with chronic diseases may explain accelerated aging phenomenon previously observed among the patients with heavy disease burden.


PURPOSE: HIV-infected individuals with non-AIDS-defining cancers are less likely to receive cancer treatment compared with uninfected individuals. We sought to identify provider-level factors influencing the delivery of oncology care to HIV-infected patients. METHODS: A survey was mailed to 500 randomly selected US medical and
radiation oncologists. The primary outcome was delivery of standard treatment, assessed by responses to three specialty-specific management questions. We used the chi(2) test to evaluate associations between delivery of standard treatment, provider demographics, and perceptions of HIV-infected individuals. Multivariable logistic regression identified associations using factor analysis to combine several correlated survey questions. RESULTS: Our response rate was 60%; 69% of respondents felt that available cancer management guidelines were insufficient for the care of HIV-infected patients with cancer; 45% never or rarely discussed their cancer management plan with an HIV specialist; 20% and 15% of providers were not comfortable discussing cancer treatment adverse effects and prognosis with their HIV-infected patients with cancer, respectively; 79% indicated that they would provide standard cancer treatment to HIV-infected patients. In multivariable analysis, physicians comfortable discussing adverse effects and prognosis were more likely to provide standard cancer treatment (adjusted odds ratio, 1.52; 95% CI, 1.12 to 2.07). Physicians with concerns about toxicity and efficacy of treatment were significantly less likely to provide standard cancer treatment (adjusted odds ratio, 0.67; 95% CI, 0.53 to 0.85). CONCLUSION: Provider-level factors are associated with delivery of nonstandard cancer treatment to HIV-infected patients. Policy change, provider education, and multidisciplinary collaboration are needed to improve access to cancer treatment.


BACKGROUND: Liver disease is common during human immunodeficiency virus (HIV) infection, but valid serum fibrosis markers are lacking. We hypothesize that HIV monoinfection and HIV/hepatitis C virus (HCV) coinfection is associated with an enhanced liver fibrosis (ELF) score higher than that for uninfected controls and examine whether this association is affected by factors other than liver injury. METHODS: The association of HIV and HIV/HCV coinfection with the ELF score was evaluated using multivariable regression after controlling for transient elastography-measured liver stiffness and traditional and HIV-related factors in a cross-sectional analysis of 297 women. RESULTS: HIV/HCV-coinfected and HIV-monoinfected women had higher median ELF scores than controls (9.6, 8.5, and 8.2, respectively). After adjustment for demographic, behavioral, and metabolic factors and for inflammatory markers, HIV/HCV coinfection remained associated with a 9% higher ELF score (95% confidence interval [CI], 5%-13%), while the association of HIV monoinfection was substantially attenuated (1% higher ELF score; 95% CI, -2% to 4%). After further adjustment for liver stiffness, HIV/HCV coinfection remained associated with 6% higher levels (95% CI, 3%-10%). In HIV/HCV-coinfected and HIV-monoinfected women, higher liver stiffness values were associated with higher ELF scores, as were older age and a nadir CD4+ T-cell count of <200 cells/mm3. CONCLUSIONS: Our findings suggest that the ELF score can be used to assess liver fibrosis severity in HIV-infected women. However, higher ELF scores may reflect extrahepatic fibrosis in HIV-infected patients with a history of severe immunosuppression or advanced age.


BACKGROUND: The prevalence of candida esophagitis (CE) might be changing in an era of highly active antiretroviral therapy (HAART) among HIV-infected patients or today's rapidly aging society among non-HIV-infected patients. However, few studies have investigated long-term CE trends, and CE risk factors have not been studied in a large sample, case-control study. This study aimed to determine long-term trends in CE prevalence and associated risk factors for patients with or without HIV infection. METHODS: Trends in CE prevalence were explored in a cohort of 80,219 patients who underwent endoscopy between 2002 and 2014. Risks for CE were examined among a subcohort of 6,011 patients. In risk analysis, we assessed lifestyles, infections, co-morbidities, immunosuppressants, and proton-pump inhibitors (PPIs). All patients were tested for HIV, hepatitis B or C virus, and syphilis infection. For HIV-infected
patients, sexual behavior, CD4 cell count, history of HAART were also assessed. RESULTS: CE prevalence was 1.7% (1,375/80,219) in all patients, 9.8% (156/1,595) in HIV-infected patients, and 1.6% (1,219/78,624) in non-HIV-infected patients. CE prevalence from 2002-2003 to 2012-2014 tended to increase in non-HIV-infected patients (0.6% to 2.5%; P<0.01) and decrease in HIV-infected patients (13.6% to 9.0%; P=0.097). Multivariate analysis revealed increasing age (odds ratio [OR], 1.02; p=0.007), HIV infection (OR, 4.92; p<0.001), and corticosteroid use (OR, 5.90; p<0.001) were significantly associated with CE, and smoking (OR, 1.32; p=0.085) and acetaminophen use (OR, 1.70; p=0.097) were marginally associated. No significant association was found with alcohol consumption, hepatitis B or C virus, syphilis, diabetes mellitus, cardiovascular disease, cerebrovascular disease, chronic kidney disease, liver cirrhosis, anticancer, or PPIs use. In HIV-infected patients, CD4 cell count <100/muL (OR, 4.83; p<0.001) and prior HAART (OR, 0.35; p=0.006) were independently associated with CE, but sexual behavior was not. Among corticosteroid users, CE was significantly associated with higher prednisone-equivalent dose (p=0.043 for trend test). CONCLUSIONS: This large, endoscopy-based study demonstrated that CE prevalence increased in non-HIV-infected patients but decreased in HIV-infected patients over 13 years. Risk analysis revealed that increasing age, HIV infection, and corticosteroids use, particularly at higher doses, were independently associated with CE, but alcohol, other infections, diabetes, anticancer drugs, and PPIs use were not.


BACKGROUND: To estimate the prevalence of vertebral fractures on chest low-dose computed tomography (LDCT) in HIV-infected smokers. METHODS: Cross-sectional study of vertebral fractures visualized on chest LDCT from a multicenter prospective cohort evaluating feasibility of chest LDCT for early lung cancer diagnosis in HIV-infected subjects. Subjects were included if 40 years or older, had been active smokers within the last 3 years of at least 20 pack-years, and had a CD4 T-lymphocyte nadir cell count <350 per microliter and an actual CD4 T-cell count >100 cells per microliter. Spinal reconstructed sagittal planes obtained from chest axial native acquisitions were blindly read by a musculoskeletal imaging specialist. Assessment of the fractured vertebra used Genant semiquantitative method. The study end point was the prevalence of at least 1 vertebral fracture. RESULTS: Three hundred ninety-seven subjects were included. Median age was 49.5 years, median smoking history was 30 pack-years, median last CD4 count was 584 cells per microliter, and median CD4 nadir count was 168 cells per microliter; 90% of subjects had a viral load below 50 copies per milliliter. At least 1 fracture was visible in 46 (11.6%) subjects. In multivariate analysis, smoking >/=40 packs-years [OR = 2.5; 95% CI: (1.2 to 5.0)] was associated with an increased risk of vertebral fracture, while HIV viral load <200 copies per milliliter [OR = 0.3; 95% CI: (0.1 to 0.9)] was protective. CONCLUSIONS: Prevalence of vertebral fractures on chest LDCT was 11.6% in this high-risk population. Smoking cessation and early introduction of antiretroviral therapy for prevention of vertebral fractures could be beneficial. Chest LDCT is an opportunity to diagnose vertebral fractures.


OBJECTIVES: The current study aimed at describing the distribution and characteristics of malignancy related deaths in human immunodeficiency virus (HIV) infected patients in 2010 and at comparing them to those obtained in 2000 and 2005. METHODS: Data were obtained from three national surveys conducted in France in 2010, 2005 and 2000. The underlying cause of death was documented using a standardized questionnaire fulfilled in French hospital wards involved in the management of HIV infection. RESULTS: Among the 728 deaths reported in 2010, 262 were cancer-related (36%). After a significant increase from 28% in 2000 to 33% in 2005 and 36% in 2010, cancers represent the leading cause of mortality in HIV infected patients. The proportion of deaths attributed to non-AIDS/non-hepatitis-related cancers significantly increased from 2000 to 2010 (11% of the deaths in 2000, 17% in 2005 and 22% in 2010, p<0.001), while those attributed to AIDS-defining cancers decreased during the same period (16% in 2000, 13% in 2005 and 9% in 2010, p = 0.024). Particularly, the proportion of respiratory cancers significantly increased from 5% in 2000 to 6% in 2005 and 11% in 2010 (p = 0.004). Lung cancer was the most common cancer-related cause of death in 2010 (instead of non-Hodgkin lymphoma so far) and represented the leading cause of death in people living with HIV overall. CONCLUSIONS: Cancer prevention (especially smoking cessation), screening strategies and therapeutic management need to be optimized in HIV-infected patients in order to reduce mortality, particularly in the field of respiratory cancers.


OBJECTIVE: Vascular aging, as assessed by structural and functional properties of the arteries, is an independent indicator of cardiovascular risk. We investigated the effect of cardiovascular risk factors (RFs) on the progression of vascular aging. DESIGN AND METHOD: One hundred and forty-two subjects (mean age 51.9 +/- 10.8 years, 94 men) attending the Peripheral Vessels Unit with no established cardiovascular disease were investigated in two examinations over a 2-year period (mean follow-up visit 1.84 years). Subjects were classified at baseline according to their number of cardiovascular RFs (from zero to two and more). The RFs were hypertension, dyslipidemia, smoking and diabetes. Subjects had at the beginning and end of the study determinations of carotid-femoral pulse wave velocity (cfPWV), aortic augmentation index corrected for heart rate (AIx75), brachial flow-mediated dilatation (FMD) and carotid intima-media thickness (cIMT). Based on these measurements the annual absolute changes were calculated. RESULTS: Subjects with more RFs had a gradual higher annual progression of cfPWV (0.092 m/s for no RF, 0.153 m/s for 1 RF and 0.316 for more than 2 RFs; p = 0.03) after adjusting for age, gender, baseline waist circumference and annual change of mean blood pressure heart rate and renal function. (Figure) Subjects with more RFs had a trend for a gradual higher annual deterioration of FMD (-0.04% for no RF, -0.14% for 1 RF and -0.51% for more than 2 RFs; p = 0.11) after adjusting for age, gender and baseline FMD. Annual progression of AIx75 between groups was not statistically significant. However, when only subjects <55 years where considered the progression rate was significantly higher in subjects with more RFs (1.04% vs. 1.52% vs. 3.15%, respectively, p = 0.02). Subjects with more RFs did not show an association with a gradual higher annual deterioration of cIMT. There was also a trend for a statistical association between the annual rate of PWV and FMD (P = 0.07).(Figure is included in full-text article.) CONCLUSIONS: : The presence of more RFs is associated with accelerated progression of vascular aging.


Combination anti-retroviral therapy (cART) for HIV-1 infection is highly effective in suppressing HIV replication, thereby preventing (or even reversing) the development of severe clinical immune deficiency and progression to the acquired immune deficiency syndrome (AIDS) and death. The success of cART has transformed HIV-1 infection from an invariably deadly infection into a chronic disease. However, HIV-infected patients on
effective cART appear to be at increased risk for (prematurely) developing a wide range of age-associated comorbidities including neurocognitive impairment. This presentation will provide an overview of the scope of the increased burden of comorbidities in HIV-infected patients on cART. Possible causative mechanisms are reviewed: (1) a high prevalence of traditional risk factors for comorbidities, e.g. lifestyle factors (smoking, alcohol, drugs), low socio-economic status, migrant health issues, and co-infections like chronic viral hepatitis and tuberculosis. (2) HIV-related factors: persistent low-level HIV replication in sanctuary sites like the brain, incomplete immune restoration, telomere shortening, chronic immune activation, immune exhaustion and senescence. And (3) cART-related factors like mitochondrial toxicity, accumulation of lamin A precursors, increased insulin resistance, dyslipidemia and decreased renal function. Current efforts of clinicians to mitigate the increased risk for comorbidities are discussed: earlier initiation of cART to prevent irreversible damage to the immune system and other organs, development of new antiretroviral agents with more favorable toxicity profiles, and more aggressive management of traditional risk factors for comorbidities. The work of the COBRA collaboration in the field of HIV-associated comorbidities is outlined and the three remaining presentations about COBRA in Session IX are briefly introduced and put into context.


Aging confers increased susceptibility to common pathogens including influenza A virus. Despite shared vulnerability to infection with advancing age in humans and rodents, the relatively long time required for immune senescence to take hold practically restricts the use of naturally aged mice to investigate aging-induced immunological shifts. Here, we show accelerated aging Lmna(Dhe) mice with spontaneous mutation in the nuclear scaffolding protein, lamin A, replicate infection susceptibility, and substantial immune cell shifts that occur with advancing age. Naturally aged (≥20 month) and 2- to 3-month-old Lmna(Dhe) mice share near identically increased influenza A susceptibility compared with age-matched Lmna(WT) control mice. Increased mortality and higher viral burden after influenza infection in Lmna(Dhe) mice parallel reduced accumulation of lung alveolar macrophage cells, systemic expansion of immune suppressive Foxp3(+) regulatory T cells, and skewed immune dominance among viral-specific CD8(+) T cells similar to the immunological phenotype of naturally aged mice. Thus, aging-induced infection susceptibility and immune senescence are replicated in accelerated aging Lmna(Dhe) mice.


BACKGROUND: The role of HIV/AIDS in non-melanoma skin cancer is not well defined. OBJECTIVES: We sought to update the evidence of the association between HIV/AIDS and risk of non-melanoma skin cancer by gender and highly active antiretroviral therapy. METHODS: We searched MEDLINE and EMBASE on 29 February 2014. Standardised incidence ratios with corresponding 95% confidence intervals were extracted and combined using generic inverse variance methods assuming a random effects model. RESULTS: Six studies including 78,794 patients with HIV/AIDS fulfilled the inclusion criteria. Analysis of all studies showed that HIV/AIDS was associated with an increased risk of non-melanoma skin cancer (standardised incidence ratio 2.76; 95% confidence interval 2.55-2.98). The standardised incidence ratios of non-melanoma skin cancer were 3.63 (1.08-12.22) for men and 2.18 (1.24-3.83) for women with HIV/AIDS, respectively. In analysis stratified by highly active antiretroviral therapy, we found that individuals receiving highly active antiretroviral therapy had lower risk of developing non-melanoma skin cancer than individuals who had not received highly active antiretroviral therapy (standardised incidence ratio, 95% confidence interval; 1.95 [1.10-3.47] versus 2.11 [1.44-3.12]). CONCLUSIONS: HIV/AIDS is associated with an increased risk of
non-melanoma skin cancer in both men and women patients. The use of highly active antiretroviral therapy appears to be beneficial in protecting against the development of non-melanoma skin cancer.


Antiretroviral therapy (ART) improved the survival of people living with HIV/AIDS (PLWHA) and decreased HIV-related morbidities. This study assesses the cancer incidence of all adult PLWHA in Israel by transmission routes before and after 1996. This cohort study was based on cross-matching the National HIV/AIDS and Cancer Registries of all HIV/AIDS and cancer cases reported from 1981 to 2010 with the National civil census. PLWHA were followed-up until cancer diagnosis, death, leaving Israel, or 2010, whichever occurred first. Cancer incidence was adjusted for age, and compared with the National incidence. Of all 5,154 PLWHA followed-up for 36,296 person-years, 362 (7.0%) developed cancer (997.4 cases per 100,000 person-years). Higher hazard ratios to develop cancer were demonstrated among older PLWHA, Jewish people, and intravenous drug users. Cancer incidence among PLWHA was higher in the pre-ART period than after 1997 (1,232.0 and 846.7 cases per 100,000 person-years, respectively). The incidence of AIDS-defining cancers was higher than non-AIDS-defining malignancies, and higher in the pre-ART than the post-ART period (777.0 and 467.2 cases per 100,000 person-years, respectively), while the incidence of non-AIDS-defining cancers showed the opposite trend (376.5 and 455.0 cases per 100,000 person-years, respectively). The incidence of AIDS-defining and non-AIDS-defining cancers declined between the pre-ART and the post-ART period by 2.0 to 3.4 times. PLWHA had higher rates of malignancies than the general population. In conclusion, cancer incidence among PLWHA was associated with age, and declined after ART introduction; yet it was higher than that of the general population. PLWHA may benefit from age-related cancer screening, increased adherence to ART, and reduction of environmental oncogenes.

Depression


HIV disclosure to sexual partners facilitates joint decision-making and risk reduction strategies for safer sex behaviors, but disclosure may be impacted by depression symptoms. Disclosure is also associated with disclosure self-efficacy, which in turn may also be influenced by depressive symptoms. This study examined the relationship between depression and HIV disclosure to partners following diagnosis among men who have sex with men (MSM), mediated by disclosure self-efficacy. Newly HIV-diagnosed MSM (n=92) who reported sexual activity after diagnosis completed an assessment soon after diagnosis which measured depressive symptoms, and another assessment within 3 months of diagnosis that measured disclosure self-efficacy and disclosure. Over one-third of the sample reported elevated depressive symptoms soon after diagnosis and equal proportions (one-third each) disclosed to none, some, or all partners in the 3 months after diagnosis. Depressive symptoms were negatively associated with disclosure self-
efficacy and disclosure to partners, while disclosure self-efficacy was positively associated with disclosure. Disclosure self-efficacy partially mediated the relationship between depression and disclosure, accounting for 33% of the total effect. These findings highlight the importance of addressing depression that follows diagnosis to enhance subsequent disclosure to sexual partners.


OBJECTIVES: We studied the incidence and prevalence of, and co-factors for depression in the Swiss HIV Cohort Study. METHODS: Depression-specific items were introduced in 2010 and prospectively collected at semiannual cohort visits. Clinical, laboratory and behavioral co-factors of incident depression among participants free of depression at the first two visits in 2010 or thereafter were analyzed with Poisson regression. Cumulative prevalence of depression at the last visit was analyzed with logistic regression. RESULTS: Among 4,422 participants without a history of psychiatric disorders or depression at baseline, 360 developed depression during 9,348 person-years (PY) of follow-up, resulting in an incidence rate of 3.9 per 100 PY (95% confidence interval (CI) 3.5-4.3). Cumulative prevalence of depression during follow-up was recorded for 1,937/6,756 (28.7%) participants. Incidence and cumulative prevalence were higher in injection drug users (IDU) and women. Older age, preserved work ability and higher physical activity were associated with less depression episodes. Mortality (0.96 per 100 PY, 95% CI 0.83-1.11) based upon 193 deaths over 20,102 PY was higher among male IDU (2.34, 1.78-3.09), female IDU (2.33, 1.59-3.39) and white heterosexual men (1.32, 0.94-1.84) compared to white heterosexual women and homosexual men (0.53, 0.29-0.95; and 0.71, 0.55-0.92). Compared to participants free of depression, mortality was slightly elevated among participants with a history of depression (1.17, 0.94-1.45 vs. 0.86, 0.71-1.03, P = 0.033). Suicides (n = 18) did not differ between HIV transmission groups (P = 0.50), but were more frequent among participants with a prior diagnosis of depression (0.18 per 100 PY, 95%CI 0.10-0.31; vs. 0.04, 0.02-0.10; P = 0.003). CONCLUSIONS: Depression is a frequent co-morbidity among HIV-infected persons, and thus an important focus of care.


Understanding the experience of depression in people living with HIV/AIDS (PLWH) could aid in the detection and treatment of the disorder. Yet, there is limited knowledge of the subjective experience of depression amongst PLWH in low- and middle-income countries despite high rates of this disorder in this population. In the current study, semi-structured interviews were conducted with depressed adults living with HIV attending a primary infectious disease clinic in South Africa. Interview transcripts were thematically analyzed. The construct of depression was consistent with DSM-IV criteria; however, the symptom presentation was distinctive. Somatic symptoms were most prominent in participants' initial presentations because participants perceived them as medically relevant. Affective, cognitive, and behavioral symptoms were not readily reported as participants did not perceive these symptoms as pertinent to their medical treatment. We identified several idioms of distress that could assist in screening for depression in this population. A valid, contextually developed screener for depression in PLWH awaits further investigation. Such a measure could play a key role in formulating a logistically feasible method of detection and treatment for depression in this population.

Barroso, J., et al. (2015). "Improvements in Depression and Changes in Fatigue: Results from the SLAM DUNC Depression Treatment Trial." AIDS Behav.
Fatigue and depression are common co-morbid conditions among people with HIV infection. We analyzed a population of HIV-infected adults with depression, who were enrolled in a depression treatment trial, to examine the extent to which improvements in depression over time were associated with improvements in HIV-related fatigue. Data for this analysis come from a randomized controlled trial to evaluate the effectiveness of improved depression treatment on antiretroviral adherence. Fatigue was measured using the HIV-Related Fatigue Scale, and depressive symptoms were measured with the Hamilton Depression Rating Scale. Participants (n = 234) were on average nearly 44 years of age and predominantly male, black or African American, and unemployed. Individuals who experienced stronger depression response (i.e., greater improvement in depression score) had larger decreases in fatigue. However, even among those who demonstrated a full depression response, nearly three-quarters continued to have either moderate or severe fatigue at 6 and 12 months.


A pilot study is underway to assess safety and acceptability of an intervention to disclose their HIV infection status to status-naive pediatric antiretroviral therapy patients in Hispaniola [the island shared by Haiti and the Dominican Republic (DR)]. Of 22 Haiti and 47 DR caregivers recruited to date, 68.2% Haiti and 34.0% DR caregivers had clinically significant depressive symptomatology at the time of enrollment (p = 0.008). Depressive symptom prevalence was higher in Haiti caregivers who were female (81.3% vs. 0 in males; p = 0.02) and in DR caregivers who were patients' mothers (50.0%) or grandmothers (66.7%; 56.0% combined) than others (9.1%), (p < 0.001). Internalized stigma was more commonly reported by Haiti (85.7%) than DR (53.2%; p = 0.01) caregivers; 56.4% of Haiti and DR caregivers reporting internalized stigma vs. 26.1% of caregivers denying it had depressive symptoms (p = 0.02). Depression is common in Hispaniola caregivers possibly affecting disclosure timing. Study participation presents opportunities for addressing caregiver depression.


South African children and adolescents living in HIV/AIDS-affected families are at elevated risk of both symptoms of anxiety and depressive symptoms. Poverty and HIV/AIDS-related stigma are additional risk factors for these negative mental health outcomes. Community level factors, such as poverty and stigma, are difficult to change in the short term and identifying additional potentially malleable mechanisms linking familial HIV/AIDS with mental health is important from an intervention perspective. HIV/AIDS-affected children are also at increased risk of bullying victimization. This longitudinal study aimed to determine whether prospective relationships between familial HIV/AIDS and both anxiety and depressive symptoms operate indirectly via bullying victimization. Adolescents (M = 13.45 years, 56.67 % female, n = 3,515) from high HIV-prevalent (>30 %) communities in South Africa were interviewed and followed-up one year later (n = 3,401, 96.70 % retention). Census enumeration areas were randomly selected from urban and rural sites in two provinces, and door-to-door sampling included all households with a resident child/adolescent. Familial HIV/AIDS at baseline assessment was not directly associated with mental health outcomes 1 year later. However, significant indirect effects operating via bullying victimization were obtained for both anxiety and depression scores. Importantly, these effects were independent of poverty, HIV/AIDS-related stigma, and baseline mental health, which highlight bullying victimization as a potential target for future intervention efforts. The implementation and rigorous evaluation of bullying prevention programs in South African communities may improve mental health outcomes for HIV/AIDS-affected children and adolescents and this should be a focus of future research and intervention.
Braithwaite, R. S., et al. (2015). "Do Alcohol Misuse, Smoking, and Depression Vary Concordantly or Sequentially? A Longitudinal Study of HIV-Infected and Matched Uninfected Veterans in Care." AIDS Behav.

We analyzed temporal patterns of alcohol misuse, smoking, and depression among veterans in care to determine whether these conditions vary concordantly or sequentially. Using the Veterans Aging Cohort Study, harmful alcohol use (AUDIT-C >/= 4), current smoking, and depression (PHQ-9 >/= 8), were measured. In regression analyses, predictors included each outcome condition at baseline, the other two conditions in the same survey, the other two conditions in the immediately preceding survey, number of years since enrollment, and HIV status. We found that current smoking and depression were more common among HIV infected individuals. Harmful alcohol use was more common among uninfected individuals. Temporal analyses suggested a concurrent pattern: each condition was associated with the other two conditions (p < 0.03, OR 1.12–1.66) as well as with the prior presence of the same condition (p < 0.0001; OR 6.38–22.02). Smoking was associated with prior depression after controlling for current depression (OR 1.16; p = 0.003). In conclusion, alcohol misuse, smoking, and depression were temporally concordant and persistent, raising the question of whether they constitute a common syndrome in HIV infected patients and others with chronic diseases.


Persons living with HIV/AIDS (PLHA) experience clinically significant pain as a result of HIV and such pain is often related to increased levels of anxiety/depression. Pain-related anxiety has been identified as a mechanism in the onset and progression of pain experience and associated affective distress. However, there has not been empirical study of pain-related anxiety in relation to affective processes among PLHA. To address this gap, hierarchical multiple regressions were conducted using SPSS v.21 to examine pain-related anxiety (as measured using the Pain Anxiety Symptoms Scale) in relation to anxiety and depressive symptoms (as measured using the Mood and Anxiety Symptoms Questionnaire) among 93 PLHA (10.8% female; Mean age = 49.63, SD = 8.89). Pain-related anxiety was significantly related to anxious arousal symptoms (beta = .43) and anhedonic depressive symptoms (beta = .25); effects were evident beyond the variance accounted for by CD4 count, race, sex, income level, and current level of bodily pain. The present results suggest that pain-related anxiety may play a role in the experience of anxiety and depressive symptoms among PLHA.


Depression and apathy are common among people living with HIV (PLWH). However, in PLWH, it is unclear whether depression and apathy are distinct conditions, which contribute to different patterns of disruption to cognitive processing and brain systems. Understanding these conditions may enable the development of prognostic indicators for HIV associated neurocognitive disorders (HAND). The present study examined substance use behavior and cognitive deficits, associated with depression and apathy, in 120 PLWH, using hierarchical regression analyses. Higher levels of depression were associated with a history of alcohol dependence and greater deficits in processing speed, motor and global cognitive functioning. Higher levels of apathy were associated with a history of cocaine dependence. It is recommended that PLWH get screened appropriately for apathy and depression, in order to receive the appropriate treatment, considering the comorbidities associated with each condition. Future research should examine the neurological correlates of apathy and depression in PLWH.

Social support has been shown to be a protective resource for mental health among chronically ill adults and caregiver populations. However, to date no known studies have quantitatively explored the relationship between social support and depression among women caring for children in HIV-endemic Southern Africa, although they represent a high risk population for mental health conditions. Using data from a household survey with 2,199 adult female caregivers of children, living in two resource-deprived high HIV-prevalence South African communities, we conducted hierarchical logistic regression analysis with interaction terms to assess whether social support had a main effect or stress-buffering effect on depression. Findings provide evidence of stress-buffering of non-HIV-related chronic illness, but not HIV-related illness. Results reinforce the importance of social support for the mental health of chronically ill caregivers, and suggest that factors related to the specific nature of HIV/AIDS may be hindering the potential stress-buffering effects of social support among people living with the disease. Implications for future research and interventions are discussed.


We examined the presence and co-occurrence of psychosocial health conditions (depression, frequent alcohol use, and victimisation) among men who have sex with men (MSM) and transgender (TG) women in India, and their cumulative association with sexual risk. A survey questionnaire was administered among a convenience sample of 600 participants (MSM = 300; TG women = 300) recruited through six non-governmental organisations in four states. Prevalences of the number of psychosocial health conditions among MSM were: none = 31.3%, one = 43%, two = 20%, and three = 5.7%; and among TG women: none = 9%; one = 35.33%, two = 38.33%, and three = 17.33%. In bivariate and multivariate models, these conditions were positively and additively related to sexual risk, providing evidence for a syndemic of psychosocial health conditions among MSM and TG women and their synergistic effect on sexual risk. In addition to the number of syndemic conditions, resilient coping and social support were significant predictors of sexual risk among MSM and TG women, respectively. HIV preventive interventions in India should screen for and address co-occurring psychosocial health conditions - experiences of violence, mental health issues, and alcohol use - among MSM and TG women.


OBJECTIVE: Major depression affects up to half of people living with HIV. However, among HIV-positive patients, depression goes unrecognized 60-70% of the time in non-psychiatric settings. We sought to evaluate three screening instruments and their short forms to facilitate the recognition of current depression in HIV-positive patients attending HIV specialty care clinics in Ontario. METHODS: A multi-centre validation study was conducted in Ontario to examine the validity and accuracy of three instruments (the Center for Epidemiologic Depression Scale [CESD20], the Kessler Psychological Distress Scale [K10], and the Patient Health Questionnaire depression scale [PHQ9]) and their short forms (CESD10, K6, and PHQ2) in diagnosing current major depression among 190 HIV-positive patients in Ontario. Results from the three instruments and their short forms were compared to results from the gold standard measured by Mini International Neuropsychiatric Interview (the "M.I.N.I."). RESULTS: Overall, the three instruments identified depression with excellent accuracy and validity (area under the curve [AUC]>0.9) and good reliability
(Kappa statistics: 0.71-0.79; Cronbach’s alpha: 0.87-0.93). We did not find that the AUCs differed in instrument pairs (p-value>0.09), or between the instruments and their short forms (p-value>0.3). Except for the PHQ2, the instruments showed good-to-excellent sensitivity (0.86-1.0) and specificity (0.81-0.87), excellent negative predictive value (>0.90), and moderate positive predictive value (0.49-0.58) at their optimal cut-points. CONCLUSION: Among people in HIV care in Ontario, Canada, the three instruments and their short forms performed equally well and accurately. When further in-depth assessments become available, shorter instruments might find greater clinical acceptance. This could lead to clinical benefits in fast-paced specialty HIV care settings and better management of depression in HIV-positive patients.


Healing Our Women (HOW) is a group-level HIV risk-reduction intervention developed to address the role of prior sexual victimization in HIV risk and protective behaviors among HIV-positive women of color. This article describes the process of adapting HOW for transgender women of color in New York City in accordance with CDC guidance for the adaptation of efficacious interventions. Twenty-one transgender women were enrolled in a study to evaluate the acceptability and fidelity of the adapted intervention, and to assess HIV knowledge, depressive symptoms, coping, condom use self-efficacy, and condom use via pre- and post-intervention surveys. We found the adapted program to be feasible to implement and acceptable to participants. We also found significant decreases in depressive symptoms and increases in positive coping from pre- to post-intervention, although replication with a larger sample and a control group comparison is needed to determine efficacy with this population.


Research assessing whether major depressive disorders (MDD) impacts neurocognitive functions in HIV+ persons has yielded inconsistent results. However, none have considered the role of MDD remission, chronicity, and stability on treatment. Ninety-five HIV+ adults clinically stable on combined antiretroviral treatment completed a psychiatric interview, a depression scale, a neuropsychological, daily living, and cognitive complaints assessments at baseline and 18 months. Participants were screened for current (within 12 months of study entry) alcohol and/or substance use disorder. History of alcohol and/or substance abuse disorder prior to the 12 months entry screen and MDD treatments were recorded. Participants were grouped into two psychiatric nomenclatures: (1) lifetime: no MDE episode (MDE), single MDE life-event treated and fully remitted, chronic MDD treated and stable, chronic MDD treated and unstable, and baseline untreated MDE; (2) recent: last 2 years MDE (yes or no). We found that lifetime and recent psychiatric history were more strongly associated with decreased in independence in daily living and cognitive complaints than with baseline neuropsychological performance. However, lack of full remission, instability on treatment in chronic MDD, and severity of symptoms in current MDE were factors in whether MDD impacted baseline neuropsychological performance. Depressive symptoms improved at follow-up in those with baseline moderate-severe symptoms, and MDD was not associated with neurocognitive change at 18 months. A history of alcohol and/or substance abuse disorder was significantly more frequent in those with treated and unstable chronic MDD but it was not associated with neuropsychological performance. MDD recurrence, chronicity profiles, and associated comorbidities are keys factors to understand any potential impact on neurocognitive abilities in HIV infection. More comprehensive consideration of these complex effects could serve at constructively updating the HAND diagnostic criteria.
The purpose of this study was to evaluate the prevalence of depressive symptoms and associated variables among people living with HIV/AIDS (PLWHA) in a specialized treatment center in a city located in southern Brazil. A cross-sectional study was conducted using the Beck Depression Inventory to assess the presence of depressive symptoms. The prevalence of depressive symptoms was 53.5% among the surveyed population, which supports the idea that depressive symptoms are more common among PLWHA, mainly if compared with the general population. It was observed that 57.7% of the study participants were with depressive symptoms and did not take any psychiatric medication and 100% did not undergo psychotherapy, which indicates undertreatment. There was no statistically significant difference in the mean CD4 count between patients with depressive symptoms (484.1 +/- 353) and patients without depressive symptoms (528.4 +/- 263). Further actions should be taken to improve the care for PLWHA. The interface between psychology, psychiatry, and internal medicine is of utmost importance to provide a more humanized care, in which the psychosocial, psychological, and psychiatric aspects are not neglected.
all types of abuse in a single model, repeated physical abuse and repeated forced sexual intercourse remained significant (AOR: 2.94, 95% CI: 1.68-5.13; AOR: 3.66, 95% CI: 1.01-13.2, respectively). DISCUSSION: These results indicate a significant association between repeated ACEs and depression in older adults. When controlling for all forms of abuse, repeated physical abuse and forced sexual intercourse are significantly correlated with late-life depression. They emphasize the need to continue developing techniques to help individuals with a history of ACEs in order to decrease their negative effects, not only immediately, but also later in life.


Patients with the HIV infection are at high risk for developing depression. The aim of this study was to investigate the safety and efficacy of antidepressant effects of minocycline on HIV patients with depression. Forty-six HIV patients, with mild-to-moderate depression and a Hamilton Depression Rating Scale (HDRS) up to 18, participated in a parallel, randomized, double-blind, placebo-controlled trial and underwent 6 weeks of treatment with either minocycline (100 mg twice daily) or placebo in the same manner. Patients were assessed using HDRS at baseline and at weeks 3 and 6. The primary outcome measure was to evaluate the efficacy of minocycline in improving depressive symptoms. General linear model repeated measures showed significant effect for time×treatment interaction on the HDRS score during the trial course [F(2, 88)=7.50, P=0.001]. There was no significant difference between the two groups regarding adverse events. No serious adverse event was reported. The administration of 100 mg minocycline twice daily seems to be safe and effective in improving depressive symptoms in HIV/AIDS patients with mild-to-moderate depression.


BACKGROUND: The aims of this study were to evaluate the prevalence of HIV and its associated demographic and clinical factors among psychiatric inpatients of a general hospital. METHODS: This was a single-center, observational, cross-sectional study that included patients consecutively admitted to our unit aged 16 years or older and with no relevant cognitive problems. The patients were evaluated using a semistructured interview and an appropriate test for HIV infection. RESULTS: Of the 637 patients who were screened, 546 (86%) who consented to participate were included in the analyses. Twenty-five (4.6%, 95% confidence interval [CI] 3.0-6.8) patients were HIV-positive. The prevalence was higher among patients with substance misuse (17.4%, 95% CI 9.7-28.8). All except one of the 25 patients knew of their seropositive condition prior to participation in the study. Only 14 (56%) of the 25 seropositive patients had previously received pharmacological treatment for their infection. According to the multiple logistic regression analysis, the likelihood of HIV infection was lower in patients with higher levels of education and higher among patients who were single, had history of intravenous drug use, and had an HIV-positive partner, particularly if they did not use condoms. Among the patients with HIV infection, 18 (72%) had a history of suicide attempts compared with 181 (34.7%) of the patients without HIV infection (relative risk 2.1, 95% CI 1.6-2.7; P<0.001). CONCLUSION: HIV infection is highly prevalent in patients admitted to a psychiatric unit, especially those with a diagnosis of substance misuse. Seropositive patients show very poor treatment adherence. The risk of suicide seems to be very high in this population. Implementing interventions to reduce the suicide risk and improve adherence to antiretroviral therapy and psychotropic medications seems crucial.

A pro-inflammatory state and a dysregulation in the tryptophan/kynurenine pathway have been documented in depression. This study examined whether treatment with the SSRI, escitalopram (ESC), could suppress inflammation and favorably shift metabolites of the kynurenine pathway in patients with major depressive disorder (MDD) within the utilized treatment period. Twenty seven healthy control subjects were included for comparison. Thirty patients were enrolled after completing baseline assessments. They received a 12-week ESC monotherapy. Twenty subjects were completers. Clinical assessments were carried out at each visit using the HAM-D, HAM-A, CGI and BDI rating scales. Blood samples were collected at each assessment and stored until analyzed. Cytokines were analyzed with Randox multiplex assay and tryptophan and kynurenine metabolites were analyzed using HPLC/GCMS. Baseline plasma concentrations of hsCRP, TNFalpha, IL6 and MCP-1 were significantly higher in patients compared to healthy controls. IL10 trended toward an increase. Baseline plasma IL1beta correlated significantly with IL1alpha, and IL4. Patients showed significant improvement in all outcome measures with a high remission rate. Significant correlations were obtained between specific symptoms and certain biomarkers at baseline but these correlations must be viewed as very preliminary. During ESC treatment concentrations of inflammatory biomarkers did not change except for TNFalpha that trended lower. Metabolites and ratios of the tryptophan/kynurenine pathway showed reductions of the neurotoxic metabolites, 3-hydroxykynurenine and quinolinic acid, 3-hydroxykynurenic acid/kynurenine, quinolinic acid/tryptophan, kynurenic acid/quinolinic acid and quinolinic acid/3-hydroxykynurenine. The results indicate that ESC may exert its antidepressant effect in part through inhibition of synthesis of certain neurotoxic kynurenine metabolites and possibly also through reduction of the inflammatory response, although there was no concordance in the time course of changes between antidepressant efficacy and reversal of the pro-inflammatory status.


HIV infection, depression, and cocaine use are independently associated with increased inflammatory signal production. There is increasing evidence about the role of inflammation in depression. In HIV disease, cocaine use may increase disease progression as well as alter T cell functioning resulting in cytokine activation and thereby increasing susceptibility to depression. We examined the association between cocaine use and depression among 447 African American persons infected with HIV who were frequent cocaine users or non-users, enrolled in an observational study in Baltimore, Maryland, between August 2003 and December 2012. The overall prevalence of depression was 40.9 % (183 of 447) participants. Among persons who were depressed, the prevalence of cocaine use was 81.4 % (149 of 183), compared to 69.3 % among persons who were not depressed (183 of 264), P = 0.004. Cocaine use was associated with nearly twofold increased odds of depression, unadjusted odds ratio (OR) 1.94, (95 % CI 1.23, 3.06); P = 0.004, compared to never using cocaine, and OR 1.02, (95 % CI 1.10, 1.05); P = 0.04 in adjusted analysis. A dose-response relationship between increasing duration of cocaine use and depression was observed. Frequency and duration of cocaine use may be associated with depression. We speculate that depression among cocaine users with HIV may involve an inflammatory component that needs further examination.


A lack of clarity on how and where case management for older adults is delivered persists, even as evidence supports its use to respond to depression. We used in-depth interviews with managers (n = 20) and staff surveys (n = 142) from 17 service agencies to explore the provision of case management services in adult day services, homecare, senior centers, and supportive housing. Limited case management services were found. Barriers included limited time...
and resources, especially for senior centers and supportive housing. Results revealed a concern about the role, feasibility, and availability of case management for older adults within these settings.


Telepsychology research has focused primarily on treatment efficacy, with far less attention devoted to how common factors relate to teletherapy outcomes. This research identified trajectories of depressive symptom relief in 105 older people living with HIV with elevated depressive symptoms enrolled in a randomized clinical trial testing two 12-session group teletherapies and compared common factors (e.g., therapeutic alliance and group cohesion) across depressive symptom trajectory groups. Growth mixture modelling of weekly depression scores identified three depressive symptom change groups: (1) 'early improvers' (31%) who reported reductions in depressive symptoms by Session 4; (2) 'delayed improvers' (16%) whose symptoms improved after Session 5 and (3) 'non-improvers' (53%). Therapeutic alliance was unrelated to treatment outcome group. Group cohesion was greater in early improvers than non-improvers. Group cohesion was unexpectedly lower, and group member similarity was greater in delayed improvers than non-improvers. Early improvers had been living with HIV/AIDS for fewer years than non-improvers. In group teletherapy, group cohesion and group member similarity are more important than client-therapist alliance. Copyright (c) 2015 John Wiley & Sons, Ltd. KEY PRACTITIONER MESSAGE: In group teletherapy with older people living with HIV (OPLWHIV), three latent outcome trajectory groups emerged over the 12-week treatment period: (1) non-improvers (53%); (2) early improvers (31%) and (3) delayed improvers (16%). In group teletherapy with OPLWHIV, group cohesion is a stronger predictor of depressive symptom relief than is client-therapist alliance. OPLWHIV in group teletherapy who do not respond to treatment until the latter therapy sessions can still experience depressive symptom relief comparable with early responders.


BACKGROUND: Given the gendered distribution of depression, this paper aims at exploring the gender disparities in the effect of depression on condom use in last sexual intercourse in a nationally representative sample of sexually active Canadians. METHODS: Data in this study came from the Canadian Community Health Survey 2009-2010 (n=124,188 aged >/=12 years). The analysis in this study was restricted to 7238 respondents aged 15-49 years who had sexual intercourse in the 12-months preceding the survey. Multivariable logistic regression, stratified by gender, was used to estimate the effect of depression on condom use adjusting for potential confounders. RESULTS: Reported condom use was lower in females (46.9%) than in males (60.9%), while depression was more in females (13.5%) than in males (8.4%). Condom use was less among people with depression, in both males and females. However, condom use was far less frequent among females (41.2%) with depression than their male counterparts (58.1%). Depression was found to reduce the odds of condom use in last sexual intercourse both in males and females. However, the effect was statistically significant in females only (adjusted odds ratio: 0.81; 95% CI: 0.66-0.99). LIMITATIONS: Cross-sectional data, and inability to capture socio-economic status and alcohol use rigorously are some of the limitations of this study. CONCLUSIONS: Depression was found to reduce condom use significantly in females. Public health programs aimed at increasing condom use should address the issues of improving self-efficacy in condom negotiation skills in females, along with addressing mental health issues, especially depression, with a gender-sensitive perspective.


An estimated 11% of the adult population in Malawi, Africa, is living with HIV/AIDS. The disease has taken a toll on communities, resulting in high morbidity and mortality. Malawian women carry the burden of being caretakers for individuals infected with HIV while also worrying about their own health. However, little is known about how HIV/AIDS affects psychological functioning among Malawian women in areas hit hardest by the epidemic. To that end, this paper examined the influence of HIV-related stigma on symptoms of anxiety and depression among 59 women 17-46 years old who were recruited from the Namitete area of Malawi. Women who reported greater worry about being infected with HIV and greater HIV-related stigma were significantly more likely to report greater symptoms of anxiety and depression. These findings suggest that interventions that reduce HIV-related stigma are likely to enhance psychological functioning among Malawian women, which in turn will improve the women's quality of life and well-being.


Previous research has identified an association between food insecurity and depression in a variety of world regions in both healthy and HIV-infected individuals. We examined this association in 183 HIV-infected Hispanic adults from the greater Boston area. We measured depression with the Burnam depression screen and food insecurity with the Radimer/Cornell Questionnaire. Dietary intake was assessed with an adapted version of the Block Food Frequency Questionnaire. Logistic regression models were created with depression as the outcome variable and food insecurity as the main predictor. In bivariate analyses, food insecurity was significantly associated with depression [odds ratio (OR) 2.5; 95% confidence interval (CI) 1.1, 5.5; p = 0.03]. When we accounted for social support, food insecurity was no longer significant. We found no differences in the quality or quantity of dietary intake between the food insecure and food secure groups. Our findings highlight the importance of social support in the association between food insecurity and depression. Food insecurity may reflect social support more than actual dietary intake in this population.


Depression and inflammation fuel one another. Inflammation plays a key role in depression's pathogenesis for a subset of depressed individuals; depression also primes larger cytokine responses to stressors and pathogens that do not appear to habituate. Accordingly, treatment decisions may be informed by attention to questions of how (pathways) and for whom (predispositions) these links exist, which are the focus of this article. When combined with predisposing factors (moderators such as childhood adversity and obesity), stressors and pathogens can lead to exaggerated or prolonged inflammatory responses. The resulting sickness behaviors (e.g., pain, disturbed sleep), depressive symptoms, and negative health behaviors (e.g., poor diet, a sedentary lifestyle) may act as mediating pathways that lead to further, unrestrained inflammation and depression. Depression, childhood adversity, stressors, and diet can all influence the gut microbiome and promote intestinal permeability, another pathway to enhanced inflammatory responses. Larger, more frequent, or more prolonged inflammatory responses could have negative
mental and physical health consequences. In clinical practice, inflammation provides a guide to potential targets for symptom management by signaling responsiveness to certain therapeutic strategies. For example, a theme across research with cytokine antagonists, omega-3 fatty acids, celecoxib, and exercise is that anti-inflammatory interventions have a substantially greater impact on mood in individuals with heightened inflammation. Thus, when inflammation and depression co-occur, treating them in tandem may enhance recovery and reduce the risk of recurrence. The bidirectional links between depression, inflammation, and disease suggest that effective depression treatments could have a far-reaching impact on mood, inflammation, and health.


In Kenya, there was a reported decline in HIV incidence and prevalence among those aged 15 to 64 years and children. Despite the decline, closer assessment of psychosocial issues like depression, contextual factors (family and community), and social support is necessary given the likely impact on overall health and HIV prevention. This paper examines an association between symptoms of depression and social support on overall health among HIV-positive participants recruited from an HIV clinic in Kenya. Descriptive statistics and logistic regression analyses were utilized. Findings reveal that compared to those with minimal depression (referent category) participants with mild, moderate, moderately severe/severe depression had higher odds of having poor health. For social support, compared with participants with no social support (referent category), participants with high social support had lower odds of having poor overall health in both unadjusted and multivariable-adjusted models. In conclusion, this study suggests that HIV clinics and interventions need to focus more on the psychological and/or mental health status of HIV-infected individuals while providing avenues such as social support groups that can be a buffer against the negative impact of HIV infection and depression on overall health outcomes.


Optimal adherence to antiretroviral therapy (ART) is key to viral suppression, but may be impeded by psychosocial consequences of HIV-infection such as stigma and depression. Measures of adherence in India have been examined in clinic populations, but little is known about the performance of these measures outside clinical settings. We conducted a cross-sectional study of 151 Tamil-speaking people living with HIV/AIDS (PLHA) in India recruited through HIV support networks and compared single item measures from the Adult AIDS Clinical Trial Group (AACTG) scale, a visual analog scale (VAS), and a question on timing of last missed dose. Depression was measured using the Major Depression Inventory (MDI) and HIV-related stigma was measured using an adaptation of the Berger Stigma Scale. Mean age was 35.6 years (SD +/- 5.9); 55.6% were male; mean MDI score was 11.9 (SD +/- 9.1); and mean stigma score was 67.3 (SD +/- 12.0). Self-reported perfect adherence (no missed doses) was 93.3% using the AACTG item, 87.1% using last missed dose, and 83.8% using the VAS. The measures had moderate agreement with each other (kappa 0.45-0.57). Depression was associated with lower adherence irrespective of adherence measure used, and remained significantly associated in multivariable analyses adjusting for age and marital status. Stigma was not associated with adherence irrespective of the measure used. The VAS captured the greatest number of potentially non-adherent individuals and may be useful for identifying PLHA in need of adherence support. Given the consistent and strong association between poorer adherence and depression, programs that jointly address adherence and mental health for PLHA in India may be more effective than programs targeting only one.

The challenges that face African American women living with HIV are immense. African American women continue to be disproportionately infected and affected by this chronic and life-threatening infection in a complex context of individual experience, interactions with the environment, formal and informal support systems, and cultural belief systems. This article identifies the Theory of Silencing the Self (STS) and a widely known model, the Social Ecological Model (SEM), as a synthesized explanatory framework in helping nurses understand how to address research questions and clinical care that is congruent with the experience of African American women living with HIV infection. In synthesizing the components of these two frameworks, an explanation of the relationship between disempowerment and depression in this population will be uncovered as a key component to making relationships at the individual, family, and community level better. Helping African American women living with HIV infection to explore and address how choosing to be silent across their life systems will advance healthcare adherence as we currently know it to improved self-management of a chronic, gender-specific, culturally-bound experience of depression.


By 2015, one-half of all HIV-positive persons in the U.S. will be 50-plus years of age, and as many as 30% of older adults living with HIV/AIDS continue to engage in unprotected sexual intercourse. Contemporary positive prevention models often include mental health treatment as a key component of HIV prevention interventions. This secondary data analysis characterized longitudinal patterns of sexual behavior in HIV-positive older adults enrolled in a randomized controlled trial of group mental health interventions and assessed the efficacy of psychosocial treatments that targeted depression to reduce sexual risk behavior. Participants were 295 HIV-positive adults >/=50 years of age experiencing mild to severe depressive symptoms, randomized to one of three study conditions: a 12-session coping improvement group intervention, a 12-session interpersonal support group intervention, or individual therapy upon request. Approximately one-fifth of participants reported one or more occasions of unprotected anal or vaginal intercourse with HIV-negative sexual partners or persons of unknown HIV serostatus over the study period. Changes in sexual behavior did not vary by intervention condition, indicating that standalone treatments that target and reduce depression may be insufficient to reduce sexual risk behavior in depressed HIV-positive older adults.


Medication adherence is highly predictive of health outcomes across chronic conditions, particularly HIV/AIDS. Depression is consistently associated with worse adherence, yet few studies have sought to understand how depression relates to adherence. This study tested three components of behavioral depression theory--goal-directed activation, positive reinforcement, and environmental punishment--as potential indirect effects in the relation between depressive symptoms and medication nonadherence among low-income, predominantly African American substance users (n = 83). Medication nonadherence was assessed as frequency of doses missed across common reasons for nonadherence. Non-parametric bootstrapping was used to evaluate the indirect effects. Of the three intermediary variables, there was only an indirect effect of environmental punishment; depressive symptoms were associated with greater nonadherence through greater environmental punishment. Goal-directed activation and positive reinforcement were unrelated to adherence. Findings suggest the importance of environmental punishment
in the relation between depression and medication adherence and may inform future intervention efforts for this population.


Depression in HIV/AIDS patients affects adherence and disease progression and often goes unnoticed. DHIVA is a cross-sectional epidemiologic survey, investigating the prevalence of depression in people living with HIV through use of a validated self-administered scale (CES-D-20), as well and the degree of concordance between the physician's perception and patients' reports. A total of 690 HIV-infected patients attending 24 centers across Italy were enrolled. Concordance was calculated by K statistics. Association between depression and subject characteristics were evaluated through univariate and multivariate logistic models (OR and 95%CI). The prevalence of depressive symptoms was 48.8% from patient's questionnaires and 49.5% from physicians' reports, with a low/fair concordance (K = .38, p < .001). CES-D-20 found severe depression in 22.5% of the patients vs 4% identified by physicians. 135/155 (87%) of the severely depressed patients (according to CES-D-20) were considered as non or mildly/moderately depressed by physicians. Risk of severe depression was associated with unemployment (p < .001), previous depression (p < .001), treatment failure (p = .001), and former smoking status (p = .018). Depression is frequent in HIV-infected patients in the HAART era, with significant discrepancy between physician perception and the self-reported CES-D-20 results. Screening should be mandatory in all HIV patients.


Human immunodeficiency virus (HIV) carries a high level of stigma to the HIV-infected individuals and their family members. Children of HIV-infected parents in China are particularly affected. The present study examined the relationship between associative stigma, self-esteem, optimism, anxiety and depression among 195 children of HIV-infected parents in rural China. Findings showed that more than one-third (35.4 %) of the participants scored higher than cut-off for depression; and 23.6-67.7 % of them scored higher than cut-off for different types of anxiety disorders. Structural equation modelling revealed that associative stigma had a significant negative relationship on self-esteem and optimism, which were associated with higher levels of depression and anxiety. The indirect effects of associative stigma on depression and anxiety were significant. The overall model showed a satisfactory fit. Findings suggest that associative stigma has a significant negative impact on mental health of children affected by HIV. Interventions to reduce their associative stigma are warranted.


BACKGROUND: Depression with pain comorbidity (DPC) has not been clearly defined among HIV positive patients in sub-Saharan Africa. It still remains a challenge despite many studies in Africa documenting a high prevalence of pain and depression among people living with HIV/AIDS. Both are associated with a grave impact on the health related outcomes in this pandemic. This study aimed at determining the prevalence, factors associated and effect on quality of life of DPC among HIV positive patients. METHODS: In a cross-sectional survey, 345 HIV positive patients were enrolled into the study. Using a pre-tested standardised questionnaire the presence of DPC was assessed after a written informed consent. The associations between DPC, quality of life, depression history, severity, and cognition were determined. A p-value of <0.05 was considered to be significant. RESULTS: Among people living
with HIV/AIDS (PLWHA), the prevalence of DPC was about 5%. PLWHA with DPC were more likely to perceive their overall quality of life as poor and scored poorly in all the domains on the WHOQOL-BREF. They were also more likely to have more severe forms of depression and recurrent episodes of depression. CONCLUSIONS: DPC is common, under diagnosed and undertreated in PLWHA in Uganda. Depression and pain screening as well as appropriate access to care for DPC have potential to improve quality of life and health outcomes. This calls for the integration and training of mental health services into HIV/AIDS care and future efforts by policy makers and HIV caregivers to address this treatment gap to advance the care of people living with HIV in Uganda.


BACKGROUND: Group support psychotherapy (GSP) is a culturally sensitive intervention that aims to treat depression by enhancing social support, teaching coping skills, and income-generating skills. We compared GSP with group HIV education (GHE) for treatment of depression in people with HIV in Uganda. METHODS: In this open-label randomised controlled trial, we included men and women with HIV, aged 19 years or older, who met the Mini International Neuropsychiatric Interview criteria for major depression from an urban HIV care centre in Kitgum district, northern Uganda. Participants were randomly assigned to receive eight weekly sessions of either GSP or GHE. Randomisation was achieved by urn (men and women separately picked a paper containing the intervention allocation from a basket; ratio 1:1), and the intervention sessions were given to gender-specific groups. Participants were followed up immediately after the intervention and 6 months after the end of treatment. The primary outcomes were change in depressive symptom scores (measured with the Self-Reporting Questionnaire) and in function scores (measured with a locally developed method), analysed by intention to treat using cluster-adjusted t tests and permutation tests. This trial is registered with The Pan African Clinical Trials Registry, number PACTR201402000742370. FINDINGS: Between Jan 6, and Jan 20, 2014, we assessed 150 individuals, of whom 109 were randomly assigned to receive eight weekly sessions of either GSP (n=57) or GHE (n=52). Change in mean depression scores immediately after intervention did not differ between groups (mean difference -0.19, 95% CI -1.77 to 1.39, p=0.78). Mean function scores did not differ between groups either (0.24, -0.41 to 0.88; p=0.41). At 6 months after end of treatment, participants in the GSP group had lower mean depression scores than did those in the GHE group (-2.50, -3.98 to 1.02, p value=0.005), and higher function scores (0.74, -0.17 to 1.65, p=0.09) than did participants in the GHE group. No adverse events were reported. INTERPRETATION: The benefits of existing HIV educational interventions in HIV care services could be improved by the addition of GSP content. Potential benefits of the integration of GSP into existing HIV interventions, such as adherence counselling or group HIV educational programmes, should be addressed in future studies. FUNDING: Grand Challenges Canada.


There are an estimated 1.1 million individuals living with HIV/AIDS in the United States. In addition to the various medical comorbidities of HIV infection, depression is one of the most frequently co-occurring psychiatric conditions among HIV-infected individuals. Furthermore, depression has been found to be associated with nonadherence to antiretroviral therapy (ART), as well as HIV disease progression. Cognitive behavioral therapy (CBT) has repeatedly been found to effectively treat depression in adult populations, and CBT for adherence and depression (CBT-AD) is an effective treatment for improving depressive symptoms and medication adherence in the context of various chronic health conditions, including diabetes and HIV-infection. This paper provides a description of the CBT-AD approach to treat depression and ART adherence in HIV-infected adults, which we have developed and tested in our clinic, and for which detailed therapist and client guides exist. To augment the description of treatment, the
present article provides video component demonstrations of several core modules that highlight important aspects of this treatment, including Life-Steps for medication adherence, orientation to CBT-AD and psychoeducation, and suggestions for adaptation of core CBT modules for HIV-infected adults. Discussion of video demonstrations highlights differences in patient presentations and course of treatment between HIV-infected adults receiving CBT-AD and HIV-uninfected adults receiving traditional CBT for depression. This description and the accompanying demonstrations are intended as a practical guide to assist therapists wishing to conduct such a treatment in the outpatient setting.


Depression is the most common psychiatric co-morbidity among people living with HIV (PLHIV), with prevalence rates ranging from 25% to 36%. Depression impacts negatively upon adherence and response to combined antiretroviral therapy (CART) and the transmission of HIV infection through increased sexually risky behavior. This cross-sectional study presents data from a reference HIV-outpatient service in Dourados (Brazil) that evaluated the association between depressive symptoms, health-related quality of life, and clinical, socioeconomic, and demographic factors in newly diagnosed HIV/AIDS patients. Using the Beck Depression Inventory (BDI), the prevalence of depressive symptoms was 61% with a predominance of self-deprecating and cognitive-affective factors. Depressive symptoms were associated with lower income (p=0.019) and disadvantaged social class (p=0.005). Poorer quality of life was related to depressive symptoms (p<0.0001), low educational level (p=0.05), and lower income (p=0.03). These data suggest that socioeconomic factors, including level of income and education, are mediating the risk of depression and poor quality of life of PLHIV. Possible explanations for this effect are discussed, including the possible role of stigma.


Depression is common among people living with HIV/AIDS (PLWHA) in sub-Saharan Africa (SSA), and can have significant consequences for HIV disease progression, treatment response and prevention. Yet mental health services are limited in most HIV care programs in this region, in part due to severe shortages of mental health professionals. To address the need for establishing an effective, sustainable model for integrating depression treatment into HIV care in SSA, we have embarked upon a 3-year research project, INDEPTH Uganda (INtegrating DEPression Treatment and in HIV care in Uganda), to evaluate a task-sharing, protocolized approach to providing antidepressant care in ten HIV clinics in Uganda. In this paper we share our experiences with two treated cases identified during the initial days of implementation, which we believe highlight the potential value and policy implications for task shifting depression care models in under-resourced settings.


OBJECTIVE: Depression is common in people living with HIV/AIDS and there is some evidence that depressive symptoms may have adverse effects on immune functioning. The purpose of this study was to determine the prevalence of current depressive disorder in patients with HIV/AIDS and its association with CD4 cell count.
METHODS: A consecutive sample of 310 patients with HIV/AIDS attending Out-patient clinic in Ahmadu Bello University Teaching Hospital (A.B.U.T.H.), Zaria, Nigeria was assessed. The Center for Epidemiologic Studies Depression Scale (CES-D) was used to screen for depressive symptoms, and the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) was used to confirm the diagnosis of current depressive disorder. The CD4 cell counts of participants with depressive disorder were compared with those of participants without depressive disorder. Multiple regression analysis was conducted to identify socio-demographic and disease-related factors associated with depression. RESULTS: Among the 310 HIV-infected participants assessed for depression, 14.2% had current depressive disorder. Adjusting for age, gender, education, occupation, and marital status, patients with CD4 counts < 150 cells/mul were more likely to be depressed. CONCLUSION: Depression is common among HIV-infected persons in Nigeria and is associated with low CD4 cell counts. The screening and treatment of mental health problems such as depression should be considered an integral component of HIV care and support.


BACKGROUND: Prevalence rates of human immunodeficiency virus (HIV) infection among the youth are disproportionately high compared to that of other age groups in Kenya. Poor mental health has been linked to risky HIV behaviour, yet few local studies have explored these aspects. This study sought to determine associations between HIV risky sexual behaviour and depression among undergraduate students at the University of Nairobi.

METHOD: A random sample of 923 (525 males and 365 females) undergraduate students was interviewed using a questionnaire to record sociodemographic variables and risky sexual behaviour including having multiple sexual partners, inconsistent condom use and engaging in sex after drinking. Depressive symptoms were measured using the Centre for Epidemiological Studies Short Depression Scale (CES-D 10). RESULTS: The students’ mean age was 23 years (s.d.4.0). Overall, 41.33% of the students scored above the cut-off point of 10 on the CES-D 10 scale, with 35.71% having moderate symptoms and 5.62% having severe depressive symptoms. The percentage of those who had ever been diagnosed with sexually transmitted infections (STIs) was 9.71% (males 8.65%; females 11.01%); and for HIV 3.04% (males 2.02%; females 4.05%). Nearly 30% reported having had multiple partners in the previous 12 months, 27.4% of the students did not use condoms with sexual partners and 21% had engaged in sex after drinking within the previous 3 months. In multivariable-bivariate logistic regression, being older, having depressive symptoms, alcohol use/binge drinking, tobacco use, sex after drinking, previous diagnosis of STI, physical abuse, sexual coercion and history of sexual abuse as a child were significantly associated with having multiple partners. Further, younger age, being female, tobacco use and previous diagnosis of STI were significantly associated with inconsistent condom use. CONCLUSION: The prevalence of HIV rate infection is low compared to the national average but risky sexual behaviour is common among the students and is positively linked to depressive symptoms among other factors. Programmes aimed at HIV prevention should be integrated with mental health interventions.


OBJECTIVE: To examine the cost-effectiveness of the HIV Translating Initiatives for Depression Into Effective Solutions (HITIDES) intervention. DESIGN: Randomized controlled effectiveness and implementation trial comparing depression collaborative care with enhanced usual care. SETTING: Three Veterans Health Administration HIV clinics in the Southern United States. SUBJECTS: Two hundred forty-nine HIV-infected patients completed the baseline interview; 123 were randomized to the intervention and 126 to usual care. INTERVENTION: HITIDES consisted of an offsite HIV depression care team that delivered up to 12 months of collaborative care. The intervention used a stepped-care model for depression treatment, and specific recommendations were based on the Texas Medication
Algorithm Project and the VA/Department of Defense Depression Treatment Guidelines. MAIN OUTCOME MEASURES: Quality-adjusted life years (QALYs) were calculated using the 12-Item Short Form Health Survey, the Quality of Well Being Scale, and by converting depression-free days to QALYs. The base case analysis used outpatient, pharmacy, patient, and intervention costs. Cost-effectiveness was calculated using incremental cost-effectiveness ratios (ICERs) and net health benefit. ICER distributions were generated using nonparametric bootstrap with replacement sampling. RESULTS: The HITIDES intervention was more effective and cost saving compared with usual care in 78% of bootstrapped samples. The intervention net health benefit was positive and therefore deemed cost-effective using an ICER threshold of $50,000/QALY. CONCLUSIONS: In HIV clinic settings, this intervention was more effective and cost saving compared with usual care. Implementation of offsite depression collaborative care programs in specialty care settings may be a strategy that not only improves outcomes for patients but also maximizes the efficient use of limited health care resources.


Both HIV infection and Methamphetamine (Meth) use disorders are associated with greater depressive symptoms and oxidative stress; whether the two conditions would show additive or interactive effects on the severity of depressive symptoms, and whether this is related to the level of oxidative stress in the CNS is unknown. 123 participants were evaluated, which included 41 HIV-seronegative subjects without substance use disorders (Control), 25 with recent (<6 months) moderate to severe Meth use disorders (Meth), 34 HIV-seropositive subjects without substance use disorders (HIV) and 23 HIV+Meth subjects. Depressive symptoms were assessed with the Center for Epidemiologic Studies-Depression Scale (CES-D), and oxidative stress markers were evaluated with glutathione (GSH), 4-hydroxynonenal (HNE), and activities of gamma-glutamyltransferase (GGT) and glutathione peroxidase (GPx) in the cerebrospinal fluid (CSF). Compared with Controls, HIV subjects had higher levels of HNE (+350%) and GGT (+27%), and lower level of GSH (-34%), while Meth users had higher levels of GPx activity (+23%) and GSH (+30 %). GGT correlated with GPx, and with age, across all subjects (p < 0.0001). CES-D scores correlated with CSF HNE levels only in Control and HIV groups, but not in Meth and HIV+Meth groups. HIV and Meth use had an interactive effects on depressive symptoms, but did not show additive or interactive effects on oxidative stress. The differential relationship between depressive symptoms and oxidative stress response amongst the four groups suggest that depressive symptoms in these groups are mediated through different mechanisms which are not always related to oxidative stress.


Adequate adherence to anti-retroviral therapy is required to achieve viral suppression and desirable treatment outcomes among HIV patients. The aim of this study was to examine the associations between adherence and severity of substance use as well as adherence and severity of depressive symptoms among Iranian HIV patients. In a prospective study, HIV patients with current substance use were assessed for adherence level via self report and pill count methods, severity of depressive symptoms (Beck Depression Inventory- II) and substance use (Addiction Severity Index) during a three months follow up after initiating antiretroviral therapy. The adherence level, severity of depressive symptoms and substance use were assessed one month, two months and three months after initiation of anti-retroviral therapy. Addiction Severity Index (ASI) composite scores were calculated for each domain and the associations between ASI domains and adherence as well as severity of depressive symptoms and adherence were assessed. Twenty six HIV patients with current substance use disorder completed the study. At the end of the first month, adherence to therapy via pill count and self-report were 80%+-31.9% and 85.12%+-32%, respectively. At the
end of the second month, adherence to therapy via pill count and self report were 87%+/-32% and 93.94%+/-23% respectively. At the end of the third month, the measured adherence via pill count and self report were 85%+/-33.7% and 90.1%+/-25.7% respectively. Adherence was higher among married patients and those who used reminder systems. Composite scores of the medical status and psychiatric status were related to higher adherence after first month. Substance use was inversely associated with adherence at the second follow up (r=-0.4, p=0.04). Also, severity of depressive symptoms was not related to adherence level. The repeated measurement analysis showed a significant decrease in psychiatric status domain of the ASI composite score after three months of initiating therapy (p=0.02). Preventive measures should aim treatment of substance use among HIV patients in order to increase adherence level. Also, conducting psychological evaluations is necessary considering the high prevalence of depression among Iranian HIV patients.


Depression and other health problems are common co-morbidities among persons living with human immunodeficiency virus infection/acquired immunodeficiency syndrome (HIV/AIDS). The aim of this study was to investigate depression, health status, and substance use in relation to HIV-infected and uninfected individuals in South Africa. Using a cross-sectional case-control design, we compared depression, physical health, mental health, problem alcohol use, and tobacco use in a sample of HIV-infected (N = 143) and HIV-uninfected (N = 199) respondents who had known their HIV status for two months. We found that depression was higher, and physical health and mental health were lower in HIV-positive than HIV-negative individuals. Poor physical health also moderated the effect of HIV infection on depression; HIV-positive individuals were significantly more depressed than HIV-negative controls, but only when general physical health was also poor. We did not find an association between alcohol or tobacco use and HIV status. These results suggest the importance of incorporating the management of psychological health in the treatment of HIV.


BACKGROUND: Depression is a major barrier to HIV treatment outcomes. OBJECTIVE: To test whether antidepressant management decision support integrated into HIV care improves antiretroviral adherence and depression morbidity. DESIGN: Pseudo-cluster randomized trial. SETTING: Four US infectious diseases clinics. PARTICIPANTS: HIV-infected adults with major depressive disorder. INTERVENTION: Measurement-based care (MBC) - depression care managers used systematic metrics to give HIV primary-care clinicians standardized antidepressant treatment recommendations. MEASUREMENTS: Primary - antiretroviral medication adherence (monthly unannounced telephone-based pill counts for 12 months). Primary time-point - 6 months. Secondary - depressive severity, depression remission, depression-free days, measured quarterly for 12 months. RESULTS: From 2010 to 2013, 149 participants were randomized to intervention and 155 to usual care. Participants were mostly men, Black, non-Hispanic, unemployed, and virally suppressed with high baseline self-reported antiretroviral adherence and depressive severity. Over follow-up, no differences between arms in antiretroviral adherence or other HIV outcomes were apparent. At 6 months, depressive severity was lower among intervention participants than usual care [mean difference -3.7, 95% confidence interval (CI) -5.6, -1.7], probability of depression remission was higher [risk difference 13%, 95% CI 1%, 25%], and suicidal ideation was lower [risk difference -18%, 95% CI -30%, -6%]. By 12 months, the arms had comparable mental health outcomes. Intervention arm participants experienced an average of 29 (95% CI: 1-57) more depression-free days over 12 months. CONCLUSION: In the largest trial of its kind among HIV-infected adults, MBC did not improve HIV outcomes, possibly because of high baseline adherence, but achieved clinically
significant depression improvements and increased depression-free days. MBC may be an effective, resource-efficient approach to reducing depression morbidity among HIV patients.


OBJECTIVE: Depression is common among patients in HIV care and is associated with worse HIV-related health behaviors and outcomes. Effective depression treatment is available, yet depression remains widely underdiagnosed and undertreated in HIV care. METHODS: As part of a multisite, randomized trial of depression treatment in HIV clinical care, the proportion of positive depression screens that resulted in study enrollment and reasons for nonenrollment were examined. RESULTS: Over 33 months, patients completed 9,765 depression screens; 19% were positive for depression, and of these 88% were assessed for study eligibility. Of assessed positive screens, 11% resulted in study enrollment. Nonenrollment after a positive screen was sometimes dictated by the study eligibility criteria, but it was often related to potentially modifiable provider- or patient-level barriers. CONCLUSIONS: Addressing patient- and provider-level barriers to engaging in depression treatment will be critical to maximize the reach of depression treatment services for HIV patients.


Depression is one of the most prevalent psychiatric comorbidities of HIV and one of the greatest barriers to HIV self-care and adherence. Despite this, little consensus exists on how to best measure depression among people living with HIV/AIDS (PLWHA) in African settings. Measurement of depression among PLWHA may be confounded by somatic symptoms. Some research recommends excluding these items to enhance measurement validity; sensitivity may be lost with this approach. We sought to characterize depression among a cohort (N = 453) of PLWHA initiating antiretroviral therapy in Uganda via factor analysis of a widely used measure of depression, the Hopkins Symptom Checklist (HSCLD). Common factor analysis was performed, associations between HSCLD and the Mental Health subscale of the Medical Outcomes Study HIV (MOS-HIV) estimated, and a Cronbach's alpha calculated to examine validity. Factor analysis yielded two factors: (1) somatic-cognitive symptoms and (2) behavioral disengagement. Persons with more versus less advanced disease (CD4 cell count of <=200 cells/mm(3)) showed no statistically significant differences in depression scores (1.7 vs. 1.7, P >/= 0.5). Both factors were significantly associated with the MOS-HIV (P < .01). Factor one was highly reliable (alpha = .81); factor two had only modest reliability (alpha = .65). Somatic-cognitive symptoms of depression and disengagement from life's activities appear to be distinct components of depression in this sample. Consideration of somatic items may be valuable in identifying depression in this setting.


Stigma and stress may place HIV-positive men who have sex with men (HIV+ MSM) at risk for depression. Additionally, HIV+ MSM might utilize multiple HIV-related services as a way to gain support for, and more effectively manage, HIV-related stressors. Although prior research has demonstrated that depression severity and utilizing support services are associated with functional or dysfunctional coping strategies, researchers have not investigated the impact of different coping combinations-specifically, the concurrent use of functional and dysfunctional strategies-in this population. Thus, we explored (1) how items on one measure of coping, the Brief COPE, capture HIV-related coping of HIV+ MSM using Principal Components Analysis, (2) how HIV+ MSM's coping groups into unique
combinations, and (3) how these coping combinations relate to depression and the scope of HIV-related support service utilization. Our sample consisted of 170 HIV+ MSM engaged with medical care. Results indicated the use of both functional and dysfunctional coping strategies. Unique combinations of functional and dysfunctional strategies showed differential associations with depression and the extent of HIV-related support service utilization. Specifically, individuals who engaged in low levels of both functional and dysfunctional coping, compared to individuals who more frequently engaged in functional coping strategies, were significantly less likely to utilize a range of critical HIV-related services. Individuals who reported frequent use of dysfunctional coping strategies, regardless of functional coping strategy use, reported higher levels of depression. Therefore, providers should continue to focus more closely on identifying functional coping strategies and reducing dysfunctional coping when working with HIV+ MSM.


BACKGROUND: MDD and HIV/AIDS have a high prevalence worldwide with severe consequences for patients. In both conditions, compliance with treatment is key to successfully treat these disorders. In the current study, we examine the effect of MDD on the compliance with ADs in patients diagnosed with co-morbid HIV/AIDS and how different classes of ADs influence compliance in this group of patients. METHODS: A prospective, cohort study design was used to analyse nationally representative medicine claims data submitted to a privately-owned South African Pharmaceutical Benefit Management (PBM) company. Two groups were distinguished in the database, namely patients with only MDD and patients with both MDD and HIV/AIDS, over a six-year study period. The study population was determined by the following inclusion criteria: patients older than 18 years, MDD should be diagnosed by a psychiatrist supported by an appropriate ICD-10 code, and all patients have to be on combination antiretroviral treatment (cARV) treatment. The medicine possession ratio (MPR) was used as proxy to determine patient compliance with AD medication. RESULTS: 127 patients (i.e. 0.24%) met the criteria of co-morbid MDD and HIV/AIDS. Females have a significantly higher prevalence of MDD and HIV/AIDS when compared to males. Patients diagnosed with both HIV/AIDS and MDD (74.43 +/- 32.03, 95% CI: 71.51-77.34) have a statistical significantly (p < 0.0001) lower compliance with AD treatment vs. MDD patients (80.94 +/- 29.44, 95% CI: 80.56-81.33), but the practical significance thereof, is low (Cohen's d = 0.2255). In this group only 26.83% of TCA had acceptable compliance compared to the 58.57% of SNRIs. Noteworthy observations were that 75% (p < 0.0217; Cramer's V = 0.0388) of venlafaxine and 28.6% (p < 0.0197; Cramer's V = -0.0705) of the paroxetine items were compliant in patients diagnosed with both HIV/AIDS and MDD. CONCLUSIONS: AD compliance is statistical significantly lower in depressed HIV/AIDS vs. depressed non-HIV/AIDS patients. However, these differences is of low practical or clinical significance, meaning that depressed HIV/AIDS patients would have missed approximately two AD doses (6.5% of a 30-day treatment period) more than the non-HIV/AIDS depressed patient over the same treatment period.


BACKGROUND: Treatment of comorbid chronic disease, such as depression, in people living with HIV/AIDS (PLWHA) increasingly falls to HIV treatment providers. Guidance in who will best respond to depression treatment and which patient-centered symptoms are best to target is limited. METHODS: Bivariable analyses were used to calculate hazard ratios for associations between baseline demographic, mental health-related, and HIV-related factors on time to first depression remission among PLWHA enrolled in a randomized trial of measurement-based antidepressant management. Time-updated factors also were analyzed at time of antidepressant (AD) initiation/adjustment and 8 weeks post AD initiation/adjustment. RESULTS: Baseline comorbid depression and anxiety; comorbid depression, anxiety and substance abuse; and generalized anxiety disorder predicted a slower time
to first remission. Being on ART but non-adherent, having panic disorder, having a history of a major depressive episode, or having been in HIV care for >10 years prior to study initiation predicted a faster time to first remission. Sleep difficulty or fatigue at the time of AD initiation/adjustment predicted a slower time to remission. In non-remitters at 8 weeks post AD initiation/adjustment, sleep difficulty, anxiety, and fatigue each predicted a slower time to remission. LIMITATIONS: Remission was determined by PHQ-9 scores, not diagnostic criteria. The results may apply only to depression recovery in this particular model of treatment. We conducted only exploratory analyses to determine magnitude of effects. CONCLUSIONS: Baseline comorbid anxiety with or without substance abuse predicts slower time to depression remission among PLWHA treated in HIV clinics. Targeting anxiety or fatigue at the time of AD initiation/adjustment or sleep difficulty, anxiety, and fatigue at 8 weeks post AD initiation/adjustment could shorten time to depression remission in this model.


Social stigma is common among men who have sex with men (MSM) across Sub-Saharan Africa, and may influence risks for HIV and sexually transmitted infections (STIs) via its association with depression. We conducted a cross-sectional study of 530 MSM in Lesotho accrued via respondent-driven sampling. Using generalized structural equation models we examined associations between stigma, social capital, and depression with condom use and testing positive for HIV/STIs. Depression was positively associated with social stigma experienced or perceived as a result of being MSM. In contrast, increasing levels of social cohesion were negatively associated with depression. Social stigma was associated with testing positive for HIV; however, this association did not appear to be mediated by depression or condom use. These data suggest a need for integrated HIV and mental health care that addresses stigma and discrimination and facilitates positive social support for MSM.


INTRODUCTION: Combined antiretroviral therapy has enabled human immunodeficiency virus (HIV) carriers to live longer. This increased life expectancy is associated with the occurrence of degenerative diseases, including HIV-associated neurocognitive disorders (HAND), which are diagnosed via a complex neuropsychological assessment. The International HIV Dementia Scale (IHDS) is a screening instrument validated in Brazil for use in the absence of neuropsychological evaluation. HIV patients are frequently diagnosed with depression. We aimed to determine the prevalence of neurocognitive impairment using the IHDS and depressive disorders using the Hamilton Rating Scale for Depression (HAM-D17), compare the IHDS performance with the performances on the Timed Gait Test (TGT), the Digit Symbol Coding Test (DS) and the Brazilian version of the Scale of Instrumental Activities of Daily Living (IADL), and evaluate the association between the IHDS performance and clinical-demographic variables. METHODS: One hundred fourteen patients were evaluated in a cross-sectional study conducted in a public outpatient clinic for infectious diseases in Marilia City, State of Sao Paulo, Brazil. Data were collected following consultation. Statistical analysis was performed in accordance with the nature and distribution of the data and hypotheses. RESULTS: According to the IHDS, 53.2% of the sampled patients were neuropsychologically impaired. According to the HAM-D17, 26.3% had depressive disorders. There were significant associations between the IHDS and the TGT and DS. Multiple regression analysis indicated that female gender, educational level, and cluster of differentiation 4 (CD4) levels were significantly and independently associated with neurocognitive impairment. CONCLUSIONS: The prevalence of neurocognitive impairment according to the IHDS is high and associated with female gender, education level, and low CD4 levels.

OBJECTIVES: The NIDA Clinical Trials Network trial of rapid HIV testing/counseling in 1281 patients was a unique opportunity to examine relationships among substance use, depressive symptoms, and sex risk behavior.

METHODS: Past 6-month substance use; substance use severity (Drug Abuse Screening Test - 10); depressive symptoms (Quick Inventory of Depressive Symptomatology); and three types of sex risk behavior (unprotected sex occasions [USOs] with primary partners; USOs with nonprimary partners; and USOs while high/drunken) were assessed. Zero-inflated negative binomial analyses provided: probability and rate of sex risk behavior (in risk behavior subsample).

RESULTS: Levels of sexual risk behavior were high, while variable across the three types of sex risk behaviors. Among the patients, 50.4% had engaged in USOs with primary partners, 42% in sex while drunk or high, and 23.8% in USOs with nonprimary partners. Similar factors were significantly associated with all three types of sex risk behaviors. For all types, problem drinking, cocaine use, and substance use severity had an exacerbating effect. Older age was associated with lower risk behavior; other relationship categories (eg, married, separated/divorced, cohabitating) were associated with greater risk behavior than was single status. Depression was associated with decreased likelihood of USOs with a primary partner. CONCLUSIONS: Sexual risk behavior is common among individuals in outpatient substance abuse treatment. Results highlight problem drinking (eg, up to three-fold) and cocaine (eg, up to twice) in increasing sex risk behavior. They demonstrate the utility of distinguishing between partner types and presence/absence of alcohol/drugs during sex. Findings argue for the need to integrate sex risk reduction into drug treatment.


CONTEXT AND OBJECTIVE: Adherence to antiretroviral treatment (ART) is not a stable condition, but is dynamic, like mental conditions. The aim of this study was to examine whether non-adherence to ART is related to demographic and immunological variables, substance use and presence of depressive symptoms. DESIGN AND SETTING: This was a cross-sectional prevalence study carried out at a public AIDS treatment center in the city of Sao Paulo, Brazil, between July 2006 and January 2007. METHODS: 438 patients on regular ART schedules with recent laboratory tests answered a demographic questionnaire, questions about substance use, the Hamilton Depression Rating Scale (HDRS) and the Simplified Medication Adherence Questionnaire (SMAQ). RESULTS: The prevalence of non-adherence over the past three months (a pattern of treatment interruption) was 46.3%, and 27.2% also reported this in the past week (a pattern of missed doses). ART interruption was significantly related to older age, lower CD4+ cell count and homosexual/bisexual transmission. The pattern of missed doses was significantly related to younger age, higher HDRS scores and higher viral load of RNA HIV. CONCLUSION: ART interruption may reflect recall errors and changes to the Brazilian demographic characteristics of HIV infection. The missed doses may reflect lifestyle characteristics of younger individuals. Attendance for HIV-positive individuals, particularly younger patients, should involve interventions and counseling in relation to the presence of depressive symptoms.


OBJECTIVE: As the advent of highly active antiretroviral therapy, HIV has become a chronic disease for most individuals in developed countries. Chronic pain is a common occurrence for HIV-infected patients and has an impact on quality of life and antiretroviral adherence. The objective of this study was to examine relationships between chronic pain and depression, substance use, mental health treatment, and pain treatment in HIV-infected patients. DESIGN: Cross-sectional study. SETTING: Three primary care sites where HIV+ patients receive treatment. SUBJECTS:
Two hundred and thirty eight HIV-infected primary care patients. METHODS: We collected self-report and chart-review information on demographics, HIV clinical status, chronic pain, depression, substance use, mental health treatment, and pain treatment. We collected data between October 2012 and November 2013. RESULTS: Of the patients enrolled in this study, 107 reported no chronic pain, 24 reported mild chronic pain, and 107 reported moderate-severe chronic pain. Participants in the moderate-severe pain group were more likely to have high levels of depressive symptoms than those in the no chronic pain group. Similarly, there was a significant relationship between chronic pain status and interference with life activities due to pain. Participants with moderate-severe chronic pain were more likely to be taking an antidepressant medication than those with mild chronic pain, and more likely to be taking a prescription opioid than the other two groups. We did not find a significant relationship between problematic substance use and chronic pain status. CONCLUSIONS: Despite pharmacologic treatment, moderate-severe chronic pain and elevated depression symptoms are common among HIV-infected patients and frequently co-occur.


OBJECTIVE: In this paper we introduce the construct of "internalized gay ageism," or the sense that one feels denigrated or depreciated because of aging in the context of a gay male identity, which we identify as an unexplored aspect of sexual minority stress specific to midlife and older gay-identified men. METHODS: Using a social stress process framework, we examine the association between internalized gay ageism and depressive symptoms, and whether one's sense of mattering mediates or moderates this association, controlling for three decades of depressive symptom histories. The sample is 312 gay-identified men (average age = 60.7 years, range = 48-78, 61% HIV-negative) participating in the Multicenter AIDS Cohort Study (MACS) since 1984/85, one of the largest and longest running studies of the natural history of HIV/AIDS in the U.S., who provided contemporary (2012/13) reports of stress experiences. RESULTS: We find that internalized gay ageism can reliably be measured among these men, is positively associated with depressive symptoms net of an array of other factors that may also influence symptomatology (including depressive symptom histories), and mattering partially mediates but does not moderate its effect on depressive symptoms. CONCLUSION: Midlife and older gay men have traversed unparalleled historical changes across their adult lives and have paved the way for younger generations of sexual minorities to live in a time of less institutionalized discrimination. Still, they are at distinct risk for feeling socially invisible and devalued in their later years.


OBJECTIVES: We assessed the relation of childhood sexual abuse (CSA), intimate partner violence (IPV), and depression to HIV sexual risk behaviors among Black men who have sex with men (MSM). METHODS: Participants were 1522 Black MSM recruited from 6 US cities between July 2009 and December 2011. Univariate and multivariable logistic regression models were used. RESULTS: Participants reported sex before age 12 years with someone at least 5 years older (31.1%), unwanted sex when aged 12 to 16 years (30%), IPV (51.8%), and depression (43.8%). Experiencing CSA when aged 12 to 16 years was inversely associated with any receptive condomless anal sex with a male partner (adjusted odds ratio [AOR] = 0.50; 95% confidence interval [CI] = 0.29, 0.86). Pressured or forced sex was positively associated with any receptive anal sex (AOR = 2.24; 95% CI = 1.57, 3.20). Experiencing CSA when younger than 12 years, physical abuse, emotional abuse, having been stalked, and pressured or forced sex were positively associated with having more than 3 male partners in the past 6 months. Among HIV-positive MSM (n = 337), CSA between ages 12 and 16 years was positively associated with having more than 3 male partners in the past 6 months.
CONCLUSIONS: Rates of CSA, IPV, and depression were high, but associations with HIV sexual risk outcomes were modest.


Experiencing sexual violence in childhood or adolescence is highly prevalent among some women living with HIV, often resulting in anxiety and depression symptoms in adulthood. Anxiety and depression have been associated with HIV medication nonadherence, yet little research has assessed distinct components of anxiety and depression as risk factors of HIV medication nonadherence. The current study examined distinct symptom components of anxiety and depression as predictors of HIV medication non-adherence among women living with HIV and childhood sexual abuse enrolled in a coping intervention. This secondary analysis included a sample of 85 women living with HIV and childhood sexual abuse and being prescribed antiretroviral medication who completed measures on anxiety, depression, and medication adherence. Results from a logistic regression analysis suggest that distinct components of anxiety may be related to medication nonadherence among this population. Targeted mental health interventions for this population may increase adherence to antiretroviral medication.


BACKGROUND: HIV-infected (HIV+) women have high rates of Gender Based Violence (GBV). Studies of GBV find that approximately 50-90% of survivors develop mood and anxiety disorders. Given that women in sub-Saharan African constitute the largest population of HIV+ individuals in the world and the regions high GBV prevalence, mental health research with HIV+ women affected by GBV (HIV+GBV+) in this region is urgently needed. METHODS: Qualitative methods were used to evaluate the mental health care needs of HIV+GBV+ female patients at an HIV clinic in the Kisumu County, Kenya. Thirty in-depth interviews and four focus groups were conducted with patients, healthcare providers and community leaders. Interviews were transcribed, translated and analyzed using qualitative data software. RESULTS: Respondents stated that physical, sexual and emotional violence against HIV+ women was widely prevalent and perpetrated primarily by untested husbands accusing a wife of marital infidelity following her positive HIV test result. Mental health problems among HIV+GBV+ women included depressive, anxiety, traumatic stress symptoms and suicidal thoughts. Participants opined that emotional distress from GBV not only caused HIV treatment default, but also led to poor HIV health even if adherent. Respondents agreed that mental health treatment was needed for HIV+GBV+ women; most agreed that the best treatment modality was individual counseling delivered weekly at the HIV clinic. LIMITATIONS: Emotional distress may be higher and/or more varied among HIV+GBV+ women who are not engaged in HIV care. CONCLUSIONS: Mental health care is needed and desired by HIV+GBV+ women in Kisumu County, Kenya.

Frailty


The growing elderly population of HIV-infected patients is leading to a significant epidemiological transition and HIV infection has been proposed as a premature and accelerated aging model rendering the individual more
susceptible to premature disability. However, the determinants of disability among this emergent population are still lacking. Therefore, the aim of this study is to determine the correlates of prevalent disability in adults \( \geq 50 \) years with HIV infection. A cross-sectional study of 184 HIV-infected adults receiving ambulatory care in an HIV clinic of a tertiary care, university-affiliated hospital in Mexico City was conducted. Disability for instrumental (IADL) and basic activities of daily living (ADL) was established. Sociodemographic factors, clinical variables, current CD4+ cell count, and HIV viral load (VL) were tested as potential determinants of disability. Multivariate logistic regression analyses were used to identify the correlates of both types of disability. The mean age was 59.3 years. All participants were receiving highly active antiretroviral therapy. Of participants 17.9% had disability for IADL and 26.1% for ADL. Multivariate logistic regression analyses indicated that being older; having a lower CD4+ cell count, and having a detectable HIV VL were independently associated with both types of disability. In addition, educational level was also independently associated with ADL disability. Age, educational level, low CD4+ cell count, and detectable HIV VL were independently associated with disability. Whether effective and timely antiretroviral therapy will reduce the risk of disability in HIV-infected elderly patients needs to be evaluated.


The frailty syndrome refers to the concurrence of a number of specific clinical manifestations that include unintentional weight loss, decreased muscle mass (sarcopenia), exhaustion, reduced physical strength and activity, and slow ambulation. It involves multiple systems, is an increasing problem in elderly populations, and is strongly associated with increases in both morbidity and mortality. Despite its recognition clinically, the frailty syndrome is not often identified in forensic situations and is only infrequently mentioned in the associated literature. As there is a direct relationship between the frailty syndrome and significant adverse health outcomes the syndrome has clear medicolegal significance.


INTRODUCTION: After the introduction of highly active antiretroviral treatment, the course of HIV infection turned into a chronic disease and most of HIV-positive patients will soon be over 50 years old. MATERIAL AND METHODS: This paper reviews the multiple aspects that physicians have to face while taking care of HIV-positive ageing patients including the definitions of frailty and the prevalence and risk factors of concomitant diseases. From a therapeutic point of view pharmacokinetic changes and antiretroviral-specific toxicities associated with ageing are discussed; finally therapeutic approaches to frailty are reviewed both in HIV-positive and negative patients. CONCLUSION AND DISCUSSION: We conclude by suggesting that the combined use of drugs with the least toxicity potential and the promotion of healthy behaviours (including appropriate nutrition and exercise) might be the best practice for ageing HIV-positive subjects.


Cytomegalovirus (CMV) is associated with poor outcomes, including physical function impairment, in older HIV-uninfected adults. Whether CMV is associated with physical functional impairment in HIV-infected adults is
unknown. The primary objective of this study was to determine the relationship between CMV-specific humoral and cell-mediated immune responses with functional impairment in well-controlled HIV infection. In a case-control study, low-function cases were matched by age, gender, and time from HIV diagnosis to high-function controls. Quantitative CMV IgG and %CMV-specific CD8(+) and CD4(+) T cells (interferon-gamma expression following CMV pp65 stimulation) were used to estimate physical function. Among 30 low-function cases and 48 high-function matched controls, CMV IgG ranged from <10 to 8,830 EU/ml, including four controls with results <10 EU/ml. Each log10 increase in CMV IgG was associated with 5-fold greater odds of low function (p=0.01); these findings were robust to adjustment for concomitant CD4(+) count, tobacco use, and age; to exclusion of subjects with CMV IgG <10 EU/ml; and to adjustment for hepatitis C viremia. %CMV-specific CD4(+) or CD8(+) T cells were not associated with low function. In bivariable models, the relationship between CMV IgG and physical function was attenuated and was no longer significant when including IL-6, CD4/CD8 ratio, or the Veterans Aging Cohort Study Index score. High levels of CMV-specific IgG were associated with impaired physical function. Attenuation of the strength of this association in bivariable models suggests an indirect relationship mediated by systemic inflammation and immune suppression.


The Veterans Aging Cohort Study (VACS) Index has previously been used to identify frail HIV-infected persons. However, data demonstrating the independent association between the VACS Index and baseline frailty status is lacking. Furthermore, the ability of the VACS Index to also reflect transitions in frailty status over time is unknown. We used data from the Study to Understand the Natural History of HIV and AIDS in the Era of Effective Therapy (SUN Study) to determine independent association of baseline frailty status with the VACS Index. We also evaluated VACS Index changes with frailty status transitions over time. We included 303 participants (median age 48 years, 76% men, 57% non-Hispanic white, 91% with plasma HIV RNA <400 copies/ml, and median CD4(+) cell count 595 cells/ml) with baseline and follow-up frailty assessments and used the Fried's criteria to define frailty status. There were 184 (61%) nonfrail, 112 (37%) prefrail, and seven (2%) frail participants at baseline. Prefrail/frailty was independently associated with a higher VACS Index score (odds ratio 1.025, p=0.019). After a median follow-up of 12 months, participants who remained prefrail/frail compared to those who remained nonfrail continued to have higher median VACS Index scores. The VACS Index score did not significantly change with transitions in frailty status over time. Our study highlights the potential utility of the VACS Index in frailty assessment within the clinical setting.


Background: Frailty is an age-related syndrome of decreased reserve and resistance to stressors, and has been associated with increased morbidity and mortality in the general population. Chronic inflammation may contribute to its development. An increased prevalence of frailty has been reported amongst HIV-infected individuals. Methods: Frailty was systematically assessed in a standardized manner in HIV-infected and otherwise comparable HIV-uninfected participants aged ≥45 years at enrolment into the AGEhIV cohort study in Amsterdam. Frailty was defined as the presence of ≥3 out of 5 factors, pre-frailty as 1–2 out of 5: 1) unintentional weight loss, 2)
low physical activity, 3) exhaustion (each by self-report), 4) time to walk 4.57 m and 5) grip-strength (each within the lowest quintile observed for the combined study population). We examined whether HIV and HIV-related characteristics were independently associated with pre-frailty and frailty by multivariable ordinal logistic regression, adjusted for potential confounders. Biologically plausible interactions were explored. Results: Data were analyzed from 570 HIV-infected and 539 HIV uninfected individuals. Overall median age was 52.4 years, 86.3% were male; median BMI in HIV-negatives and HIV-positives was 24.2 and 24.5 kg/m² (p = 0.02). Median known duration of HIV infection was 11.9 years. 94.6% of HIV-infected were currently on cART, of whom 96.7% had undetectable HIV-1 RNA (b40 c/mL). Prevalence rates of frailty (11.1% vs. 3.2%) and pre-frailty (50.5% vs. 36.2%) were significantly higher in HIV-infected individuals (p b 0.001). HIV-infected individuals scored significantly worse for all 5 factors. HIV infection remained statistically significantly associated with (pre-)frailty after adjustment for potentially confounding determinants (Table 1). Gender, region of origin, other comorbidity than mentioned in the table, heavy alcohol intake or IDU were not associated. Soluble (s)CD163, but not hs-CRP, D-dimer or sCD14, was associated with (pre-)frailty. Lower BMI was associated with (pre-)frailty in HIV-infected, but not in HIV-uninfected individuals (p(interaction) = 0.005). Within the HIV-positives, duration of having CD4 b 200/mm³, but not nadir CD4 count or history of AIDS, was associated with (pre-)frailty (OR 1.17/year, 95% CI 1.03–1.33). This association no longer remained significant following adjustment for lowest ever recorded BMI or weight loss 5 kg, and duration of protease inhibitor (PI) use (Table 2). Conclusions: HIV infection was independently associated with a higher prevalence of frailty and pre-frailty in middle-aged HIV infected patients compared to HIV-uninfected controls. The observed independent association amongst HIV-positives with ever recorded lowest BMI or weight loss, rather than indicators of immunodeficiency, could be indicative of HIV-associated wasting being the more important driver of frailty development in HIV.


Background: Association of frailty with adverse clinical outcomes has been reported in Western countries, but data from the Asian population are scarce. This study aimed to evaluate the epidemiology of frailty among community-dwelling middle-aged and elderly population and to explore its association with musculoskeletal health in Taiwan. Methods: I-Lan Longitudinal Aging Study (ILAS) data were retrieved for this study. Frailty was defined by the Fried’s criteria; a comparison of demographic characteristics, physical performance, and body composition, including skeletal muscle mass and bone mineral density (BMD), as well as recent falls, history of hip fractures and the functional status of subjects with different frailty statuses were accomplished. Results: Overall, the data of 1,839 participants (mean age: 63.9±9.3 years, male 47.5%) were obtained for analysis. The prevalence of pre-frailty was 42.3% in men and 38.8% in women, whereas the prevalence of frailty was 6.9% and 6.7% in men and women, respectively. Frailty was significantly associated with older age, the male gender, larger waist circumference, lower skeletal muscle index, lower hip BMD, poorer physical function, poorer nutritional status, and poorer cognitive function. Also, frailty was significantly associated with osteoporosis (OR: 7.73, 95% CI: 5.01–11.90, p<0.001), history of hip fractures (OR: 8.66, 95% CI: 2.47–30.40, p = 0.001), and recent falls (O.R: 2.53, 95% CI: 1.35–4.76, p = 0.004).

Conclusions: Frailty and pre-frailty, in Taiwan, was closely associated with recent falls, history of hip fractures and osteoporosis among community-dwelling people 50 years of age and older. Furthermore, frailty intervention programs should take an integrated approach towards strengthening both and muscle mass, as well as prevention of falls. [ABSTRACT FROM AUTHOR]

Our aim was to determine whether baseline measures of cognitive functioning, walking speed, and depressive status are independent predictors of limitations in instrumental activities of daily living (IADL) in older adults. The cross-sectional study involved 1329 community-dwelling adults, aged 75 years or older. At baseline, the Mini-Mental State Examination (MMSE), Symbol Digit Substitution Test (SDST), Geriatric Depressive Scale (GDS), and a word list memory task were completed, and self-reported IADLs and walking speed were recorded. The longitudinal study involved 948 participants without baseline IADL limitation, which was assessed at baseline and 15-month follow up, using the three Kihon Checklist subitems. In cross-sectional analyses, participants with IADL limitation demonstrated greater GDS scores, slower walking speeds, and lower MMSE, word list memory task, and SDST (only for women) scores relative to those without IADL limitation. In the longitudinal analyses, baseline walking speed (men: OR 0.98; women: OR 0.97, p<0.05) and word list memory task scores (men: OR 0.84; women: OR 0.83, p<0.05) in both sexes and SDST scores in women (OR 0.96, p=0.04) were independent predictors of subsequent IADL limitation. Walking speed, memory, and processing speed may be independent predictors of IADL limitation in older adults.


Claims of accelerated or premature aging are frequently made. However, the lack of standard criteria for measuring speed of aging makes such claims highly questionable. Because of fundamental gaps in our current understanding of the biological mechanisms of aging, the development of specific phenotypes that are due to aging is difficult and such phenotypes can only be derived by observational data. However, a clinical phenotype of aging exists that is experienced by all living individuals and is pervasive across multiple physiologic systems. Characterizing this phenotype can serve as a basis for measuring the speed of aging, and can facilitate a better understanding of the aging process and its interaction with chronic diseases.


Background: Implementation fidelity, the degree to which a care program is implemented as intended, can influence program impact. Since results of trials that aim to implement comprehensive care programs for frail, older people have been conflicting, assessing implementation fidelity alongside these trials is essential to differentiate between flaws inherent to the program and implementation issues. This study demonstrates how a theory-based assessment of fidelity can increase insight in the implementation process of a complex intervention in primary elderly care. Methods: The Geriatric Care Model was implemented among 35 primary care practices in the Netherlands. During home visits, practice nurses conducted a comprehensive geriatric assessment and wrote a tailored care plan. Multidisciplinary team consultations were organized with the aim to enhance the coordination between professionals caring for a single patient with complex needs. To assess fidelity, we identified 5 key intervention components and formulated corresponding research questions using Carroll's framework for fidelity. Adherence (coverage, frequency, duration, content) was assessed per intervention component during and at the end of the intervention period. Two moderating factors (participant responsiveness and facilitation strategies) were assessed at the end of the intervention. Results: Adherence to the geriatric assessments and care plans was high, but decreased over time. Adherence to multidisciplinary consultations was initially poor, but increased over time. We found that individual differences in adherence between practice nurses and primary care physicians were moderate, while differences in participant responsiveness (satisfaction, involvement) were more distinct. Nurses deviated from protocol due to contextual factors and personal work routines. Conclusions: Adherence to the Geriatric Care Model was high for most of the essential intervention components. Study limitations include the limited number of assessed moderating factors. We argue that a longitudinal investigation of adherence per intervention component is essential for a
complete understanding of the implementation process, but that such investigations may be complicated by practical and methodological challenges. Trial registration: The Netherlands National Trial Register (NTR). Trial number: 2160.

[ABSTRACT FROM AUTHOR]

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BACKGROUND: Serum markers of inflammation increase with age and have been strongly associated with adverse clinical outcomes among both HIV-infected and uninfected adults. Yet, limited data exist on the predictive and clinical utility of aggregate measures of inflammation. This study sought to evaluate the relationship of a recently validated aggregate inflammatory index with frailty and mortality among aging HIV-infected and uninfected injection drug users. METHODS: Frailty was assessed among HIV-infected and uninfected participants in the AIDS Linked to the IntraVenous Experience (ALIVE) cohort study using the five Fried phenotypic criteria: weight loss, exhaustion, low physical activity, decreased grip strength, and slow gait. The aggregate inflammatory index was constructed from serum measures of interleukin-6 and soluble tumor necrosis factor-alpha receptor-1. Multinomial logistic regression was used to assess the relationship of frailty with inflammation. Cox proportional hazards models were used to estimate risk for all-cause mortality. RESULTS: Among 1,326 subjects, the median age was 48 years and 29% were HIV-infected. Adjusting for sociodemographics, comorbidity, and HIV status, frailty was significantly associated with each standard deviation increase in log interleukin-6 (odds ratio 1.33; 95% CI, 1.09-1.61), log tumor necrosis factor-alpha receptor-1 (odds ratio 1.25; 95% CI, 1.04-1.51) and inflammatory index score (odds ratio 1.39; 95% CI, 1.14-1.68). Adjusting for sociodemographics, comorbidity, HIV status, and frailty, the inflammatory index score was independently associated with increased mortality (HR 1.65; 95% CI, 1.44-1.89). CONCLUSION: A recently validated, simple, biologically informed inflammatory index is independently associated with frailty and mortality risk among aging HIV-infected and uninfected injection drug users.


The inclusion of latent frailties in survival models can serve two purposes: (1) the modelling of dependence in clustered data, (2) explaining lack of fit of univariate survival models, like deviation from the proportional hazards assumption. Multi-state models are somewhere between univariate data and clustered data. Frailty models can help in understanding the dependence in sequential transitions (like in clustered data) and can be useful in explaining some strange phenomena in the effect of covariates in competing risks models (like in univariate data). The (im)possibilities of frailty models will be exemplified on a data set of breast cancer patients with death as absorbing state and local recurrence and distant metastasis as intermediate events.

Men with human immunodeficiency virus (HIV) infection are often hypogonadal and develop several HIV-associated non-acquired immunodeficiency syndrome (AIDS) (HANA) conditions that impair overall health status. No studies explored the relationship between health status and serum testosterone (T) in HIV-infected men. This study aims to investigate the association between total serum T and HANA, multimorbidity, and frailty in a large cohort of 1359 HIV-infected men and to explore the relationship between patients' overall health status and serum T. Among biochemical and hormonal measurement performed the main are serum total T, free triiodothyronine (fT3), and luteinizing hormone. Other outcome measurements include anthropometry, assessment of comorbidities and disabilities, overall health status defined as the number of HANA and by the 38-item multimorbidity frailty index, anthropometry, and bone mineral density. The cumulative relative risk of comorbidities is increased in HIV-infected men with hypogonadism (p < 0.001) and hypogonadism is associated with several comorbidities. The prevalence of hypogonadism increases progressively with the increase of the number of comorbidities. Frailty index is inversely related to serum total T (age-adjusted r = 0.298, r(2) = 0.089, p < 0.0001). Serum fT3 levels are significantly lower in hypogonadal than eugonadal men (p = 0.022). This suggests that low serum T could be considered a sensitive marker of frailty and poor health status and that the latter might induce hypogonadism. The more HIV-infected men are frail the more they are hypogonadal. This suggests that hypogonadism might be a naturally occurring condition in unhealthy HIV-infected men and raises concern about the safety of T treatment. In conclusion, low serum T is associated with multimorbidity, HANA, and frailty in HIV-infected men and this association seems to be bidirectional. Given the wide attitude to offer T treatment to HIV-infected men, caution is needed when prescribing T to HIV-infected male patients, especially if the patient is unhealthy or frail.


Frailty is a complex and heterogeneous clinical syndrome. Cognitive frailty has been considered as a subtype of frailty. In this study, we refine the definition of cognitive frailty based on existing reports about frailty and the latest progress in cognition research. We obtain evidence from the literature regarding the role of pre-physical frailty in pathological aging. We propose that cognitive impairment of cognitive frailty results from physical or pre-physical frailty and comprises two subtypes: the reversible and the potentially reversible. Reversible cognitive impairment is indicated by subjective cognitive decline (SCD) and/or positive fluid and imaging biomarkers of amyloid-beta accumulation and neurodegeneration. Potentially reversible cognitive impairment is MCI (CDR=0.5). Based on the severity of cognitive impairment, it is possible to determine the primary and secondary preventative measures for cognitive frailty. We further determine whether SCD is a component of pre-clinical AD or the early stage of other neurodegenerative diseases, which is required for guiding personal clinical intervention.


BACKGROUND: Gait speed predicts functional decline, disability, and death and is considered a biomarker of biological aging. Changes in gait speed in persons aging with HIV may provide an important method of gauging health and longevity in an under assessed population. The objective of this study was to evaluate and quantify the rate of gait speed decline in HIV-infected (HIV(+)) men compared with HIV-uninfected (HIV(-)) men. METHODS: The study was nested in the Multicenter AIDS Cohort Study. The primary outcome was usual gait speed in meters per second measured between 2007 and 2013. Differences in the rate of gait speed decline and the incidence of clinically slow gait (<1.0 m/s) were assessed using multivariate linear regression models and Cox proportional hazards models, respectively. RESULTS: A total of 2025 men (973 HIV(+)) and 1052 HIV(-)) aged 40 years and older contributed 21,187 person-visits (9955 HIV(+)) and 11,232 HIV(-)) to the analysis. Average gait speeds at the age 50 years were 1.24 and
1.19 m/s in HIV(-) and HIV(+) men, respectively (P < 0.001). In fully adjusted models, gait speed decline averaged 0.009 m/s per year after age 50 years (P < 0.001); this decline was 0.025 m/s per year greater in HIV(+) men (P < 0.001). Moreover, HIV(+) men had a 57% greater risk of developing clinically slow gait (adjusted hazard ratio = 1.57, 95% confidence interval: 1.27 to 1.91). CONCLUSIONS: These findings indicate a faster rate of functional decline in HIV-infected men, suggesting greater risks of disability and death with advancing age.


BACKGROUND: Nutritional status and food insecurity are associated with frailty in the general U.S. population, yet little is known about this in the aging population of people living with HIV (PLWH). OBJECTIVES: Given the potential importance of nutrition and the amenability to intervention, we examined the association between nutritional status, food insecurity, and frailty in PLWH. DESIGN: Cross sectional study. SETTING: Boston, Massachusetts, U.S.A. PARTICIPANTS: 50 PLWH, age >/=45 years, recruited from a cohort study examining risk factors for cardiovascular disease. MEASUREMENTS: Frailty, duration of HIV, use of antiretroviral therapy, disease history, food insecurity, physical function, and physical activity were assessed by questionnaire. Dietary intake was assessed using 3-day food records. Blood was drawn for CD4+ cell count, hemoglobin, hematocrit, and lipid levels. Physical measurements included height, weight, and skinfold thickness. RESULTS: The prevalence of frailty was 16% (n=8), 44% were pre-frail (n=22) and 40% were not frail (n=20). The number of reported difficulties with 20 activities of daily living was highest in frail (mean 10.4+/−3.9 SD), followed by pre-frail (6.5+/−4.6), and lowest in not frail participants (2.0+/−2.3). Seven (88%) of the frail PLWH lost weight with an average weight loss of 22.9 pounds; 6 (75%) reported unintentional weight loss, and all 6 of these met the frailty criteria for weight loss of 10 or more pounds. Nine (45%) of the not frail PLWH reported losing weight with an average weight loss of 6.2 pounds; 5 (23%) reported unintentional weight loss of <10 pounds. Frail PLWH were more likely to report being food insecure than not frail PLWH (63% vs. 10%, p=0.02), and tended to have lower energy intake than not frail PLWH. CONCLUSION: Research is needed on targeted interventions to improve food security and activities of daily living in PLWH for both the prevention and improvement of frailty.


Modern medical management of comorbid conditions has resulted in escalating use of multiple medications and the emergence of the twin phenomena of multimorbidity and polypharmacy. Current understanding of how the polypharmacy in conjunction with multimorbidity influences trauma outcomes is limited, although it is known that trauma patients are at increased risk for medication-related adverse events. The comorbidity-polypharmacy score (CPS) is a simple clinical tool that quantifies the overall severity of comorbidities using the polypharmacy as a surrogate for the "intensity" of treatment necessary to adequately control chronic medical conditions. Easy to calculate, CPS is derived by counting all known pre-injury comorbid conditions and medications. CPS has been independently associated with mortality, increased risk for complications, lower functional outcomes, readmissions, and longer hospital stays. In addition, CPS may help identify older trauma patients at risk of post-emergency department undertriage. The goal of this article was to review and refine the rationale for CPS and to provide an evidence-based outline of its potential clinical applications.

A chronic disease in older adults usually runs a course that is less predictable than in younger individuals. Unexplained variations in disease incidence, prognosis, therapeutic responses, and toxicity are frequently observed among older adults. This heterogeneity poses huge challenges to the current one-size-fits-all health care systems, and calls for more personalized managements of chronic diseases in older adults. Aging is characterized by progressive deterioration of bodily functions with increasing risk of failure over time. The entire process is hierarchically organized, and progresses from intracellular events to changes at systemic and ultimately organism levels at different rates among different individuals. Aging biology exerts great influences on the development and progression of most age-related chronic diseases. Thus, aging biology could contribute to the complexity of illnesses that increase with age, and aging biomarkers possess a great potential to enable personalized health risk assessment and health care. We review evidences supporting the roles of aging biomarkers in risk assessment of prevalent age-related diseases.

Frailty phenotype is an objectively measured indicator of advanced-stage aging that is characterized by organism-level dysfunction. In contrast, altered inflammation markers level signifies an earlier stage between cellular abnormalities and systems dysfunction. Results of human observational studies and randomized controlled trials indicate that these measures, albeit simple, greatly facilitate classification of older patients with cancer, chronic kidney disease, cardiovascular diseases and type 2 diabetes mellitus into groups that vary in disease incidence, prognosis and therapeutic response/toxicity. As the detailed mechanisms underlying the complex biologic process of aging are unraveled in the future, a larger array of biomarkers that correlate with biologic aging at different stages will be discovered. Following the translational research framework described in this article, these research efforts would result in innovations in disease prevention and management that address the huge unmet health needs of aging populations.

Neuro-cognition


Marked improvements in survival and health outcome for people infected with HIV have occurred since the advent of combination antiretroviral therapy over a decade ago. Yet HIV-associated neurocognitive disorders continue to occur with an alarming prevalence. This may reflect the fact that infected people are now living longer with chronic infection. There is mounting evidence that HIV exacerbates age-associated cognitive decline. Many middle-aged HIV-infected people are experiencing cognitive decline similar that to that found among much older adults. An increased prevalence of vascular and metabolic comorbidities has also been observed and is greatest among older adults with HIV. Premature age-associated neurocognitive decline appears to be related to structural and functional brain changes on neuroimaging, and of particular concern is the fact that pathology indicative of neurodegenerative disease has been shown to occur in the brains of HIV-infected people. Yet notable differences also exist between the clinical presentation and brain disturbances occurring with HIV and those occurring in neurodegenerative conditions such as Alzheimer’s disease. HIV interacts with the aging brain to affect neurological structure and function. However, whether this interaction directly affects neurodegenerative processes, accelerates normal cognitive aging, or contributes to a worsening of other comorbidities that affect the brain in older adults remains an open question. Evidence for and against each of these possibilities is reviewed.
Antiretroviral therapy has increased the life span of HIV+ individuals; however, HIV-associated neurocognitive disorder (HAND) occurrence is increasing in aging HIV patients. Previous studies suggest HIV infection alters autophagy function in the aging CNS and HIV-1 proteins affect autophagy in monocyte-derived cells. Despite these findings, the mechanisms leading to dysregulated autophagy in the CNS remain unclear. Here we sought to determine how HIV Tat dysregulates autophagy in neurons. Tat caused a dose-dependent decrease in autophagosome markers, microtubule-associated protein-1 light chain beta II (LC3II), and sequestosome 1 (SQSTM1), in a membrane-enriched fraction, suggesting Tat increases autophagic degradation. Bafilomycin A1 increased autophagosome number, LC3II, and SQSTM1 accumulation; Tat cotreatment diminished this effect. Tat had no effect when 3-methyladenine or knockdown of beclin 1 blocked early stages of autophagy. Tat increased numbers of LC3 puncta and resulted in the formation of abnormal autophagosomes in vitro. Likewise, in vivo studies in GFAP-Tat tg mice showed increased autophagosome accumulation in neurons, altered LC3II levels, and neurodegeneration. These effects were reversed by rapamycin treatment. Tat colocalized with autophagosome and lysosomal markers and enhanced the colocalization of autophagosomes with lysosomal markers. Furthermore, co-IP studies showed that Tat interacts with lysosomal-associated membrane protein 2A (LAMP2A) in vitro and in vivo, and LAMP2A overexpression reduces Tat-induced neurotoxicity. Hence, Tat protein may induce autophagosome and lysosome fusion through interaction with LAMP2A leading to abnormal neuronal autophagy function and dysregulated degradation of critical intracellular components. Therapies targeting Tat-mediated autophagy alterations may decrease neurodegeneration in aging patients with HAND.


OBJECTIVE: To evaluate the role of neurocognitive impairment on retention in care across the lifespan in antiretroviral-naive persons newly diagnosed with HIV. DESIGN: A prospective observational study of 138 antiretroviral-naive newly diagnosed HIV-positive participants who presented to an urban clinic between August 2010 and April 2013. METHODS: All participants underwent a baseline evaluation that included a neuromedical examination and brief neuropsychological test battery. Retention in care was operationalized as attending at least two visits separated by more than 90 days during the 12-month follow-up period. RESULTS: Fifty-five per cent of participants were retained in care over the study observation period. In a logistic regression controlling for ethnicity, there was a significant interaction between age and neurocognitive impairment in predicting retention in care (P = 0.009). Planned post-hoc analyses showed that neurocognitive impairment was associated with a significantly lower likelihood of retention in care among participants aged 50 years and older (P = .007), but not among younger participants (P > 0.05). CONCLUSION: Extending prior research on antiretroviral adherence and medication management, findings from this study indicate that neurocognitive impairment may be an especially salient risk factor for poor retention in care among older adults with newly diagnosed HIV infection.


The increased prevalence of HIV among adults >50 years underscores the importance of improving our understanding of mechanisms causing HIV-associated neurocognitive disorders (HAND). Identifying novel and noninvasive diagnostic predictors of HAND prior to clinical manifestation is critical to ultimately identifying means of preventing progression to symptomatic HAND. Here, using a task-switching paradigm, in which subjects were cued (unpredictably) to perform a face-gender or a word-semantic task on superimposed face and word images, we
examined the behavioral and neural profile of impaired cognitive control in older HIV+ adults (N = 14, 9 HIV+). Functional magnetic resonance imaging (fMRI) and behavioral data were acquired while subjects were performing the face-gender or word-semantic task. We found that, despite comparable performance in standard neuropsychology tests that are designed to probe executive deficits, HIV-infected participants were significantly slower than uninfected controls in adapting to change in task demand, and the behavioral impairments can be quantitatively related to difference in fMRI signal at the dorsal anterior cingulate cortex (ACC). Due to the limited sample size of this hypothesis-generating study, we should take caution with these findings and future studies with a large and better matched sample size are needed. However, these rather novel findings in this study have a few important implications: first, the prevalence of cognitive impairments in HIV+ older adults might be even higher than previously proposed; second, ACC (in particularly its dorsal region) might be one of the key regions underlying cognitive impairments (in particularly executive functions) in HIV; and third, it might be beneficial to adopt paradigms developed and validated in cognitive neuroscience to study HAND, as these techniques might be more sensitive to some aspects of HIV-associated neurocognitive impairments than standard neuropsychology tests.


HIV infection leads to age-related conditions in relatively young persons. HIV-associated neurocognitive disorders (HAND) are considered among the most prevalent of these conditions. To study the mechanisms underlying this disorder, researchers need an accurate method for measuring biological aging. Here, we apply a recently developed measure of biological aging, based on DNA methylation, to the study of biological aging in HIV+ brains. Retrospective analysis of tissue bank specimens and pre-mortem data was carried out. Fifty-eight HIV+ adults underwent a medical and neurocognitive evaluation within 1 year of death. DNA was obtained from occipital cortex and analyzed with the Illumina Infinium Human Methylation 450K platform. Biological age determined via the epigenetic clock was contrasted with chronological age to obtain a measure of age acceleration, which was then compared between those with HAND and neurocognitively normal individuals. The HAND and neurocognitively normal groups did not differ with regard to demographic, histologic, neuropathologic, or virologic variables. HAND was associated with accelerated aging relative to neurocognitively normal individuals, with average relative acceleration of 3.5 years. Age acceleration did not correlate with pre-mortem neurocognitive functioning or HAND severity. This is the first study to demonstrate that the epigenetic age of occipital cortex samples is associated with HAND status in HIV+ individuals pre-mortem. While these results suggest that the increased risk of a neurocognitive disorder due to HIV might be mediated by an epigenetic aging mechanism, future studies will be needed to validate the findings and dissect causal relationships and downstream effects.


Our aim was to determine whether baseline measures of cognitive functioning, walking speed, and depressive status are independent predictors of limitations in instrumental activities of daily living (IADL) in older adults. The cross-sectional study involved 1329 community-dwelling adults, aged 75 years or older. At baseline, the Mini-Mental State Examination (MMSE), Symbol Digit Substitution Test (SDST), Geriatric Depressive Scale (GDS), and a word list memory task were completed, and self-reported IADLs and walking speed were recorded. The longitudinal study involved 948 participants without baseline IADL limitation, which was assessed at baseline and 15-month follow up, using the three Kihon Checklist subitems. In cross-sectional analyses, participants with IADL limitation demonstrated greater GDS scores, slower walking speeds, and lower MMSE, word list memory task, and SDST (only for women)
scores relative to those without IADL limitation. In the longitudinal analyses, baseline walking speed (men: OR 0.98; women: OR 0.97, p<0.05) and word list memory task scores (men: OR 0.84; women: OR 0.83, p<0.05) in both sexes and SDST scores in women (OR 0.96, p=0.04) were independent predictors of subsequent IADL limitation. Walking speed, memory, and processing speed may be independent predictors of IADL limitation in older adults.


The Veterans Aging Cohort Study (VACS) Index was developed as a risk index for health outcomes in HIV, and it has been consistently associated with mortality. It shows a significant, yet relatively weak, association with neurocognitive impairment, and little is known about its utility among ethnic/racial minority groups. We examined whether the association between the VACS Index and neurocognition differed by ethnic/racial group. Participants included 674 HIV-infected individuals (369 non-Hispanic whites, 111 non-Hispanic blacks, and 194 Hispanics). Neurocognitive function was assessed via a comprehensive battery. Scaled scores for each neurocognitive test were averaged to calculate domain and global neurocognitive scores. Models adjusting for demographics and HIV disease characteristics not included in the VACS Index showed that higher VACS Index scores (indicating poorer health) were significantly associated with worse global neurocognition among non-Hispanic whites. This association was comparable in non-Hispanic blacks, but nonsignificant among Hispanics (with similar results for English and Spanish speaking). We obtained comparable findings in analyses adjusting for other covariates (psychiatric and medical comorbidities and lifestyle factors). Analyses of individual neurocognitive domains showed similar results in learning and delayed recall. For other domains, there was an effect of the VACS Index and no significant interactions with race/ethnicity. Different components of the VACS Index were associated with global neurocognition by race/ethnicity. In conclusion, the association between the VACS Index and neurocognitive function differs by ethnic/racial group. Identifying key indicators of HIV-associated neurocognitive impairment by ethnic/racial group might play an important role in furthering our understanding of the biomarkers of neuroAIDS.


High rates of cognitive impairment persist in human immunodeficiency virus (HIV) infection, despite improved health outcomes and reduced mortality through widespread use of antiretroviral therapy (ART). Heavy alcohol use and cigarette smoking are potential contributors to neurocognitive impairment in people living with HIV (PLWH), yet few studies have examined their influence concurrently. Here we investigated the effects of self-reported alcohol use and smoking on learning, memory, processing speed, verbal fluency, and executive function in 124 HIV-positive men who have sex with men [age (mean +/- SD) = 42.8 +/- 10.4 years], engaged with medical care. All participants were heavy drinkers. Duration of HIV infection averaged 9.9 +/- 7.6 years, and 92.7% were on a stable ART regimen. Participants completed a neuropsychological battery and assessment of past 30-day substance use. Average number of drinks per drinking day (DPDD) was 5.6 +/- 3.5, and 33.1% of participants were daily smokers. Rates of neurocognitive impairment were the highest in learning (50.8%), executive function (41.9%), and memory (38.0%). Multiple regression models tested DPDD and smoking status as predictors of neurocognitive performance, controlling for age and premorbid intelligence. Smoking was significantly, negatively related to verbal learning (p = .046) and processing speed (p = .001). DPDD was a significant predictor of learning (p = .047) in a model that accounted for the interaction of DPDD and smoking status. As expected, premorbid intelligence significantly predicted all neurocognitive scores (ps < .01), and older age was associated with slower processing speed (ps < .01). In conclusion, smoking appears to be associated with neurocognitive functioning deficits in PLWH beyond the effects of heavy
drinking, aging, and premorbid intelligence. Smoking cessation interventions have the potential to be an important target for improving functional outcomes in heavy drinking PLWH.


 Older HIV-infected adults have a higher risk of neurocognitive impairment, but the underlying mechanisms are poorly understood. Here, we investigated the associations between levels of HIV DNA in peripheral blood, soluble markers of inflammation and cellular trafficking in blood and cerebrospinal fluid (CSF) and neurocognitive functioning among 18 younger (22-40 years) and 26 older (50-71 years) HIV-infected subjects, who were administered a comprehensive neurocognitive battery. Older HIV-infected individuals presented higher levels of inflammation in CSF and blood compared to younger individuals, but no difference was observed in HIV DNA levels. Among older participants, higher HIV DNA levels were significantly associated with more severe neurocognitive impairment (p = 0.005), particularly in the Executive Functions domain (p = 0.004). No association was observed between HIV DNA and neurocognition among younger individuals. Despite significantly increased inflammation observed in the older group, none of the inflammatory markers were associated with neurocognitive impairment among older HIV+ individuals (p > 0.05). Our study supports the involvement of peripheral HIV DNA reservoir in the pathogenesis of neurocognitive disorder during suppressive ART. Correlates of neurocognitive impairment might differ between younger and older adults, suggesting that future treatment and prevention strategies for HIV-associated neurocognitive disorders likely need to be tailored based on age.


 Older individuals often experience declines in cognitive function after events (e.g. infection, or injury) that trigger activation of the immune system. This occurs at least in part because aging sensitzes the response of microglia (the brain's resident immune cells) to signals triggered by an immune challenge. In the aging brain, microglia respond to these signals by producing more pro-inflammatory cytokines (e.g. interleukin-1beta or IL-1beta) and producing them for longer than microglia in younger brains. This exaggerated inflammatory response can compromise processes critical for optimal cognitive functioning. Interleukin-1beta is central to the inflammatory response and is a key mediator and modulator of an array of associated biological functions; thus its production and release is usually very tightly regulated. This review will focus on the impact of dysregulated production of IL-1beta on hippocampus dependent-memory systems and associated synaptic plasticity processes. The neurotrophin brain-derived neurotrophic factor (BDNF) helps to protect neurons from damage caused by infection or injury, and it plays a critical role in many of the same memory and hippocampal plasticity processes compromised by dysregulated production of IL-1beta. This suggests that an exaggerated brain inflammatory response, arising from aging and a secondary immune challenge, may erode the capacity to provide the BDNF needed for memory-related plasticity processes at hippocampal synapses. This article is part of a Special Issue entitled 'Neuroimmunology and Synaptic Function'.


Frailty is a complex and heterogeneous clinical syndrome. Cognitive frailty has been considered as a subtype of frailty. In this study, we refine the definition of cognitive frailty based on existing reports about frailty and the latest progress in cognition research. We obtain evidence from the literature regarding the role of pre-physical frailty
in pathological aging. We propose that cognitive impairment of cognitive frailty results from physical or pre-physical frailty and comprises two subtypes: the reversible and the potentially reversible. Reversible cognitive impairment is indicated by subjective cognitive decline (SCD) and/or positive fluid and imaging biomarkers of amyloid-beta accumulation and neurodegeneration. Potentially reversible cognitive impairment is MCI (CDR=0.5). Based on the severity of cognitive impairment, it is possible to determine the primary and secondary preventative measures for cognitive frailty. We further determine whether SCD is a component of pre-clinical AD or the early stage of other neurodegenerative diseases, which is required for guiding personal clinical intervention.


OBJECTIVE: This study aimed to determine the combined effects of age and HIV infection on the risk of incident neurocognitive disorders. METHOD: A total of 146 neurocognitively normal participants were enrolled at baseline into one of four groups based on age (< 40 years and ≥ 50 years) and HIV serostatus resulting in 24 younger HIV-, 27 younger HIV+, 39 older HIV-, and 56 older HIV+ individuals. All participants were administered a standardized clinical neuropsychological battery at baseline and 14.3 +/- 2 months later. RESULTS: A logistic regression predicting incident neurocognitive disorders from HIV, age group, and their interaction was significant (chi(2)(4) = 13.56, p = .009), with a significant main effect of HIV serostatus (chi(2)(1) = 5.01, p = .025), but no main effect of age or age by HIV interaction (ps > .10). Specifically, 15.7% of the HIV+ individuals had an incident neurocognitive disorder as compared to 3.2% of the HIV- group (odds ratio = 4.8 [1.2, 32.6]). Among older HIV+ adults, lower baseline cognitive reserve, prospective memory, and verbal fluency each predicted incident neurocognitive disorders at follow-up. CONCLUSIONS: Independent of age, HIV infection confers a nearly fivefold risk for developing a neurocognitive disorder over approximately one year. Individuals with lower cognitive reserve and mild weaknesses in higher-order neurocognitive functions may be targeted for closer clinical monitoring and preventative measures.


As the population of older Latinos in the U.S. increases, availability of culturally adapted geriatric psychiatry services is becoming a growing concern. This issue is exacerbated for rural Latino populations. In this study, we assessed whether neurocognitive assessment via telepsychiatry (TP) using a Spanish-language battery would be comparable to in-person (IP) testing using the same battery in a sample of Spanish-speaking older adults in a rural setting. Patients (N = 22) received IP and TP testing 2 weeks apart. The order of IP and TP test administrations in individual subjects was determined randomly. Comparison of scores indicated that there were no significant differences between IP and TP test performance though both groups scored non-significantly higher at the second visit. This study demonstrates feasibility and utility of neurocognitive testing in Spanish using TP among older rural Latinos.


OBJECTIVES: Deficits in cognitive function remain prevalent in HIV-infected individuals. The aim of this European multicentre study was to assess factors associated with cognitive function in antiretroviral therapy (ART)-naive HIV-infected subjects at the time of enrolment in the NEAT 001/Agence Nationale de Recherche sur le SIDA (ANRS) 143 study. METHODS: Prior to starting ART, seven cognitive tests exploring domains including episodic memory, verbal fluency, executive function and psychomotor speed were administered with scores standardized to z-score using the study population sample mean and standard deviation. The primary measure was overall z-score average (NPZ). We assessed associations between baseline factors and test results using multivariable regression models. RESULTS: Of 283 subjects with baseline cognitive assessments, 90% were male and 12% of black ethnicity. Median (interquartile range) age, years of education, years of known HIV infection, baseline CD4 count and baseline HIV RNA were 39 (31, 47) years, 13 (11, 17) years, 1 (0, 4) years, 344 (279, 410) cells/μL and 4.74 (4.28, 5.14) log10 HIV-1 RNA copies/mL, respectively. Forty per cent were current smokers. Factors significantly associated with poorer overall cognitive performance in multivariable models included older age, shorter duration of education, black ethnicity, lower height, and lower plasma HIV RNA. CONCLUSIONS: In this large, European-wide, ART-naive population with relatively preserved immunity and early HIV infection, cognitive function scores at the time of ART initiation were associated with demographic and HIV-disease factors.

Polypharmacy


Male-to-female transgender women experience high rates of substance use and HIV. A recent substance use trend is the use of prescription medication without a doctor's consent. No research to date has examined the associations between this non-medical use of prescription drugs and HIV risk behaviour in transgender women. In the present study, transgender women recruited from community venues (N = 104) in the Mid-Atlantic region of the United States completed surveys assessing demographic information, non-medical use of prescription drugs, other substance use, injection practices and sexual risk behaviour. Twenty-four per cent of the sample reported lifetime non-medical use of prescription drugs across the following categories: analgesics (21.2%), anxiolytics (14.4%), stimulants (12.5%) and sedatives (8.7%). Participants reporting non-medical use of prescription drugs were more likely to report other substance use, needle use to inject drugs, injecting silicone and sharing needles. In multivariable analyses, non-medical use of prescription drugs was associated with unprotected sex, sex after engaging in substance use, and commercial sex work, after controlling for demographic factors. Self-esteem and social support from family served as protective factors for non-medical use of prescription drugs. HIV-prevention programmes focused on transgender women in the United States may wish to expand their assessment of substance use to include the use of prescription medications without a physician's consent.
Patients with human immunodeficiency virus (HIV) are living longer with their disease, as HIV has become a chronic illness managed with combination antiretroviral therapy (cART). This has led to an increasing number of patients greater than 50 years old living successfully with HIV. As the number of older adults with HIV has increased, there are special considerations for the management of HIV. Older adults with HIV must be monitored for drug side effects and toxicities. Their other non-HIV comorbidities should also be considered when choosing a cART regimen. Older adults with HIV have unique issues related to medication compliance. They are more likely than the younger HIV patients to have vision loss, cognitive impairment, and polypharmacy. They may have lower expectations of their overall health status. Depression and financial concerns, especially if they are on a fixed income, may also contribute to noncompliance in the aging HIV population.


Medication adherence and persistence is recognized as a worldwide public health problem, particularly important in the management of chronic diseases. Nonadherence to medical plans affects every level of the population, but particularly older adults due to the high number of coexisting diseases they are affected by and the consequent polypharmacy. Chronic disease management requires a continuous psychological adaptation and behavioral reorganization. In literature, many interventions to improve medication adherence have been described for different clinical conditions, however, most interventions seem to fail in their aims. Moreover, most interventions associated with adherence improvements are not associated with improvements in other outcomes. Indeed, in the last decades, the degree of nonadherence remained unchanged. In this work, we review the most frequent interventions employed to increase the degree of medication adherence, the measured outcomes, and the improvements achieved, as well as the main limitations of the available studies on adherence, with a particular focus on older persons.


OBJECTIVE: The increasing population of human immunodeficiency virus (HIV)-infected elderly patients results in a higher number of comorbidities and greater incidence of polypharmacy in addition to antiretroviral therapy (ART). The aim of this study is to describe the use of concomitant medication in older HIV-infected patients and to compare it with older general population. METHODS: The study included HIV-positive outpatients (>49 years) who received ART in 2011. Co-medication dispensed by pharmacies in that year was collected. Defined daily dose (DDD) for each drug was calculated by patient. A comparison was made between the use of co-medication among men between 50 and 64 years old in general population against the HIV-infected population. RESULTS: The study was based on 118 patients (77% men), of which 82% took at least one co-medication and 58% at least five. The commonest co-medications used by HIV-positive patients were antibiotics (44%); analgesics (44%); anti-inflammatories (39%); antacids (38%); and psycholeptics (38%). The medicines used for the greatest number of days per HIV-positive patient were those related to the renin-angiotensin system; anti-diabetics; lipid modifying agents; antithrombotics; and calcium channel blockers. In comparison with the general male population, a higher proportion of HIV-infected patients used antibiotics (42 vs 30%, P = 0.018), antiepileptics (16 vs 5%, P = 0.000), psycholeptics (35 vs 17%, P = 0.000) and COPD medications (14 vs 7%, P = 0.008). The duration of antibiotics and psycholeptic use in HIV-infected patients was longer compared to the general population (P < 0.05). CONCLUSIONS: Older HIV-positive
patients frequently take a higher number of co-medications, which increases the risk of adverse events, interactions with other medications, and may lead to poorer treatment adherence.


Highly active antiretroviral therapy has helped to improved control of the HIV infection, and has led to a progressively older population with the infection having a life expectancy quite similar to that of the general population. On the other hand, it is also known that HIV infection, even in patients with undetectable viral loads and good immunity, carries an increased cardiovascular risk, as well as an increased incidence of certain cancers. Therefore, the majority of HIV-infected patients receive several drugs (either prescribed by the physician or self-administered) combined with antiretrovirals. This article reviews the interactions between antiretrovirals and other drugs that can cause significant damage to patients, or even be life-threatening and of whom clinicians, especially those not directly treating HIV-infected patients, should be aware. A review is also presented on the implications of interactions between antiretrovirals and other drugs in special situations, such as the co-administration with cytostatics, immunosuppressants used in solid organ transplantation, or patients receiving new treatments for hepatitis C. Generally, combinations with two nucleos(t)ide reverse transcriptase inhibitors and raltegravir (or in the near future, dolutegravir) are those with less potential for clinically significant interactions.


Persons living with HIV (PLWH) may be at increased risk for polypharmacy (>5 concomitant medications) over non-PLWH, presumably due to antiretroviral therapy (ART). Potential concerns associated with polypharmacy include clinically significant drug-drug interactions, adverse drug reactions, increased pill burden, and rising treatment-related costs. Our objective was to evaluate prescription of multiple non-ART medications to PLWH, compared to non-PLWH, in US outpatient clinics and to identify factors associated with polypharmacy. Cross-sectional data from the 2006-2010 National Hospital Ambulatory Medical Care Survey were used for this study. Visits for PLWH were identified using HIV ICD9-CM codes 042, V08, and 079.53. Patients < 18 years of age were excluded. Relevant demographics included sex, age, race/ethnicity, and insurance status, while comorbid conditions included hypertension, diabetes, and hyperlipidemia. Multivariate logistic regression analyses evaluated factors independently associated with prescription of >5 medications. In total, 7,360,000 weighted visits for PLWH (13% aged 18-29 y; 55% aged 30-49 y; 32% aged >50 y) and 374,626,000 weighted visits for non-PLWH (18% aged 18-29 y; 32% aged 30-49 y; 50% aged >50 y) met study criteria. The greatest prevalence of hypertension, diabetes, and hyperlipidemia was in those >50 years of age (p < .001 for all comorbidities in PLWH and non-PLWH). In 2006, 16% of PLWH were prescribed >5 medications, doubling to 35% in 2010. In 2006, 24% of non-PLWH were prescribed >5 medications, only increasing to 32% in 2010. Older age (30-49 y and >50 y) was associated with >5 prescription medications in PLWH (adjusted odds ratio [aOR] = 2.538, 95% CI; 1.31-4.918 and aOR = 2.703, 95% CI; 1.678-4.354) and in non-PLWH (aOR = 2.546, 95% CI; 2.235-2.9 and aOR = 5.208, 95% CI; 4.486-6.047), respectively. Prescription of multiple medications is on the rise in PLWH, more so than in non-PLWH. Additional research is needed to explore how prescription of multiple medications differentially affects younger PLWH vs. older PLWH.

BACKGROUND: The population infected with HIV is getting older and these people will increasingly develop age-related non-communicable diseases (NCDs). We aimed to quantify the scale of the change and the implications for HIV care in the Netherlands in the future. METHODS: We constructed an individual-based model of the ageing HIV-infected population, which followed patients on HIV treatment as they age, develop NCDs—including cardiovascular disease (hypertension, hypercholesterolaemia, myocardial infarctions, and strokes), diabetes, chronic kidney disease, osteoporosis, and non-AIDS malignancies—and start co-medication for these diseases. The model was parameterised by use of data for 10,278 patients from the national Dutch ATHENA cohort between 1996 and 2010. We made projections up to 2030. FINDINGS: Our model suggests that the median age of HIV-infected patients on combination antiretroviral therapy (ART) will increase from 43.9 years in 2010 to 56.6 in 2030, with the proportion of HIV-infected patients aged 50 years or older increasing from 28% in 2010 to 73% in 2030. In 2030, we predict that 84% of HIV-infected patients will have at least one NCD, up from 29% in 2010, with 28% of HIV-infected patients in 2030 having three or more NCDs. 54% of HIV-infected patients will be prescribed co-medications in 2030, compared with 13% in 2010, with 20% taking three or more co-medications. Most of this change will be driven by increasing prevalence of cardiovascular disease and associated drugs. Because of contraindications and drug-drug interactions, in 2030, 40% of patients could have complications with the currently recommended first-line HIV regimens. INTERPRETATION: The profile of patients in the Netherlands infected with HIV is changing, with increasing numbers of older patients with multiple morbidities. These changes mean that, in the near future, HIV care will increasingly need to draw on a wide range of medical disciplines, in addition to evidence-based screening and monitoring protocols to ensure continued high-quality care. These findings are based on a large dataset of HIV-infected patients in the Netherlands, but we believe that the overall patterns will be repeated elsewhere in Europe and North America. The implications of such a trend for care of HIV-infected patients in high-burden countries in Africa could present a particular challenge. FUNDING: Medical Research Council, Bill & Melinda Gates Foundation, Rush Foundation, and Netherlands Ministry of Health, Welfare and Sport.


Modern medical management of comorbid conditions has resulted in escalating use of multiple medications and the emergence of the twin phenomena of multimorbidity and polypharmacy. Current understanding of how the polypharmacy in conjunction with multimorbidity influences trauma outcomes is limited, although it is known that trauma patients are at increased risk for medication-related adverse events. The comorbidity-polypharmacy score (CPS) is a simple clinical tool that quantifies the overall severity of comorbidities using the polypharmacy as a surrogate for the "intensity" of treatment necessary to adequately control chronic medical conditions. Easy to calculate, CPS is derived by counting all known pre-injury comorbid conditions and medications. CPS has been independently associated with mortality, increased risk for complications, lower functional outcomes, readmissions, and longer hospital stays. In addition, CPS may help identify older trauma patients at risk of post-emergency department undertriage. The goal of this article was to review and refine the rationale for CPS and to provide an evidence-based outline of its potential clinical applications.
Renal


BACKGROUND: Chronic kidney disease (CKD) is frequent in individuals infected with human immunodeficiency virus (HIV). Progression to end-stage renal disease can be slowed by appropriate medical management. METHODS: To assess whether active promotion of guidelines improves CKD management, we conducted a cluster randomized controlled trial within the French Hospital Database on HIV (FHDH-ANRS CO4). We randomized 46 centers participating in the FHDH to either simple information on guideline availability or active promotion with a multifaceted and repeated intervention comprising reminders and audit feedback and targeting of local opinion leaders carried out between April 2009 and April 2010. Outcome measure was CKD management adequacy assessed before and 2 years after the beginning of the intervention in HIV-infected patients with moderate to severe CKD. CKD management was considered adequate in case of referral to a nephrologist or if proteinuria, blood pressure, low-density lipoprotein cholesterol level, and glycemia had been measured during the previous year and medications had been prescribed when necessary. RESULTS: Three hundred six patients were enrolled, of whom 238 (78%) completed the 2 years of follow-up. During the study period, the percentage of patients receiving adequate CKD management improved from 64.1% to 70.4% (+6.3%) in the active arm and from 68.3% to 75.6% (+7.3%) in the control arm (adjusted mean difference, -0.7 percentage points [95% confidence interval: -9.2 to 7.9]; P = .95). The biggest impact of active promotion was on the management of proteinuria and blood pressure. CONCLUSIONS: Adequate compliance with CKD management guidelines improved slightly between 2009 and 2011, with no difference between the simple information and active promotion arms. CLINICAL TRIALS REGISTRATION: CCTIRS 10.150 and CNIL DR-2010-379.


BACKGROUND: Human immunodeficiency virus (HIV)-infected individuals are at higher risk for chronic kidney disease than HIV-uninfected individuals. We investigated whether the inflammation present in treated HIV infection contributes to kidney dysfunction among HIV-infected men receiving highly active antiretroviral therapy. METHODS: The glomerular filtration rate (GFR) was directly measured (using iohexol) along with 12 markers of inflammation in Multicenter AIDS Cohort Study participants. Exploratory factor analysis was used to identify inflammatory processes related to kidney dysfunction. The estimated levels of these inflammatory processes were used in adjusted logistic regression analyses evaluating cross-sectional associations with kidney function outcomes. RESULTS: There were 434 HIV-infected men receiving highly active antiretroviral therapy and 200 HIV-uninfected men. HIV-infected men were younger (median age, 51 vs 53 years) and had higher urine protein-creatinine ratios (median, 98 vs 66 mg/g) but comparable GFRs (median, 109 vs 106 mL/min/1.73 m(2)). We found an inflammatory process dominated by markers: soluble tumor necrosis factor receptor 2, soluble interleukin 2 receptor alpha, soluble gp130, soluble CD27, and soluble CD14. An increase of 1 standard deviation in that inflammatory process was associated with significantly greater odds of GFR </=90 mL/min/1.73 m(2) (odds ratio, 2.0) and urine protein >200 mg/g (odds ratio, 2.3). CONCLUSIONS: Higher circulating levels of immune activation markers among treated HIV-infected men may partially explain their higher burden of kidney dysfunction compared with uninfected men.

BACKGROUND: Chronic renal failure and HIV/AIDS are both prevalent in Nigeria. We performed a cross-sectional analysis of renal function in newly diagnosed, treatment-naive HIV-infected patients before initiating highly active antiretroviral therapy. METHODS: Treatment-naive patients were recruited. Patients with diabetes mellitus and hypertension were excluded. Plasma creatinine level was used to measure the estimated glomerular filtration rate [(eGFR) by Modification of Diet in Renal Disease equation]. Predictors of creatinine and eGFR were determined by univariate and multivariate analyses. RESULTS: We evaluated 183 patients. In all, 44 (24%) patients had a GFR <60 mL/min/1.73 m², implying moderate chronic kidney disease (CKD). Considering the eGFR, 22 (12%) patients had stage 1, 117 (63.9%) stage 2, 13 (7.1%) stage 3, 27 (14.8%) stage 4, and 4 (2.2%) stage 5 CKD. Creatinine inversely correlated with CD4 (r = -.228, P = .025). CD4 predicts creatinine (odds ratio 1.6, 95% confidence interval 1.0-1.8, P = .003). CONCLUSION: In ART-naive patients, CKD is common, and low eGFR was associated with lower CD4 counts.


Antiretroviral therapy has markedly reduced acquired immune deficiency syndrome-related deaths and opportunistic infectious diseases. This has resulted in prolonged survival of individuals infected with the human immunodeficiency virus (HIV). However, this improvement in survival has been accompanied by an increase in the incidence of chronic kidney disease (CKD) and end-stage renal disease. CKD is now epidemic among HIV-infected populations in both Western and Eastern countries. Risk factors associated with CKD in HIV-infected populations include aging, hypertension, diabetes mellitus, co-infection with hepatitis C virus, a low CD4 cell count, and a high HIV viral load. Clinical experience has shown that HIV-infected individuals often have one or more concurrent risk factors for CKD. The cumulative effect of multiple risk factors on the development of CKD should be noted in this population. Glomerular disease directly related to HIV infection, so-called HIV-associated nephropathy, remains an important cause of CKD among a limited HIV population of African descent, but is less likely to be common among other urban HIV populations. The impact of exposure to nephrotoxic antiretroviral agents on the development of kidney disease is both an old and a new concern. In particular, the association of tenofovir with kidney tubular injury has been an area of great interest. The findings regarding tenofovir's adverse effect on long-term kidney function vary among studies. The early identification and treatment of CKD is recommended for reducing the burden of patients requiring dialysis in HIV-infected populations. Periodic monitoring of urinary concentrations of albumin, protein, and tubular injury markers such as low-molecular-weight proteins may be useful for the early diagnosis of patients at risk for incident CKD. This review focuses on recent epidemiology, clinical characteristics, and management of CKD in a contemporary HIV-infected population.


OBJECTIVES: HIV-related renal diseases are the leading causes of chronic kidney diseases worldwide. The present study aimed to investigate the prevalence of pathological proteinuria and its risk factors among HIV patients. METHODS: A review of the medical records of 666 HIV-infected individuals aged 18 years or older in an urban HIV/AIDS clinic based in Porto Alegre in southern Brazil. Overt proteinuria was defined as a protein-to-creatinine ratio greater than 150 mg/g according to Kidney Disease: Improving Global Outcomes. RESULTS: The prevalence of
pathological proteinuria in the present study cohort was 20%. Characteristics associated with pathological proteinuria after univariate analysis included alcohol abuse, hepatitis C virus coinfection, the occurrence of diabetes and therapy including tenofovir. Adjusted residuals analysis indicated an association between pathological proteinuria and both a CD4 lymphocyte count below 200 cells/mm³ and a viral load higher than 1000 copies/mL. Additionally, an absence of pathological proteinuria was associated with a CD4 lymphocyte count higher than 500 cells/mm³. After adjustment for variables with p<0.2 in the univariate analysis using a Poisson regression model, tenofovir-containing regimens and a CD4 lymphocyte count below 200 cells/mm³ were significantly associated with pathological proteinuria.

CONCLUSION: The risk of chronic kidney diseases in this large contemporary cohort of HIV-infected individuals appeared to be attributable to a combination of HIV-related risk factors. In addition to the traditional risk factors cited in the literature, both regimens containing tenofovir and HIV disease severity seem to be associated with chronic kidney diseases in patients with HIV. Assessment of proteinuria constitutes a novel method for chronic kidney disease staging in HIV-infected individuals and may be effectively used to stratify the risk of progression to end-stage renal disease.


Life expectancy among HIV-infected (HIV+) individuals has improved dramatically with effective antiretroviral therapy. Consequently, chronic diseases such as end-stage liver and kidney disease are growing causes of morbidity and mortality. HIV+ individuals can have excellent outcomes after solid organ transplantation, and the need for transplantation in this population is increasing. However, there is a significant organ shortage, and HIV+ individuals experience higher mortality rates on transplant waitlists. In South Africa, the use of organs from HIV+ deceased donors (HIVDD) has been successful, but until recently federal law prohibited this practice in the United States. With the recognition that organs from HIVDD could fill a critical need, the HIV Organ Policy Equity (HOPE) Act was passed in November 2013, reversing the federal ban on the use of HIV+ donors for HIV+ recipients. In translating this policy into practice, the biologic risks of using HIV+ donors need to be carefully considered. In this mini-review, we explore relevant aspects of HIV virology, antiretroviral treatment, drug resistance, opportunistic infections and HIV-related organ dysfunction that are critical to a transplant team considering HIV-to-HIV transplantation.


BACKGROUND: Adding gender-related modifiable characteristics or behaviors to the Veterans Aging Cohort Study (VACS) index might improve the accuracy of predicting mortality among HIV-infected women on treatment. We evaluated the VACS index in women with HIV, determined whether additional variables would improve mortality prediction, and quantified the potential for improved survival associated with reduction in these additional risk factors. METHODS: The VACS index (based on age, CD4 count, HIV-1 RNA, hemoglobin, aspartate aminotransferase, alanine aminotransferase, platelets, creatinine, and Hepatitis C status) was validated in HIV-infected women in the Women’s Interagency HIV Study (WIHS) who initiated antiretroviral therapy between January 1996 and December 2007. Models were constructed adding race, depression, abuse, smoking, substance use, transactional sex, and comorbidities to determine whether predictability improved. Population attributable fractions were calculated. RESULTS: The VACS index accurately predicted 5-year mortality in 1057 WIHS women with 1 year on highly active antiretroviral therapy with c-index 0.83 [95% confidence interval (CI): 0.79 to 0.87]. In multivariate analysis, the VACS index score [adjusted hazard ratio (aHR) for a 5-point increment 1.30; 95% CI: 1.25 to 1.35], depressive symptoms (aHR 1.73; 95% CI: 1.17 to 2.56), and history of transactional sex (aHR 1.93; 95% CI: 1.33 to 1.82) were independent statistically significant predictors of mortality. CONCLUSIONS: Both depression and transactional sex significantly
improved the performance of the VACS index in predicting mortality among HIV-infected women. Providing treatment for depression and addressing economic and psychosocial instability in HIV-infected women would improve health and perhaps point to a broader public health approach to reducing HIV mortality.


**BACKGROUND:** Existing data suggest that human immunodeficiency virus (HIV)-infected African Americans carrying 2 copies of the APOL1 risk alleles have greater risk of kidney disease than noncarriers. We sought to determine whether HIV RNA suppression mitigates APOL1-related kidney function decline among African Americans enrolled in the Multicenter AIDS Cohort Study. **METHODS:** We genotyped HIV-infected men for the G1 and G2 risk alleles and ancestry informative markers. Mixed-effects models were used to estimate the annual rate of estimated glomerular filtration rate (eGFR) decline, comparing men carrying 2 (high-risk) vs 0-1 risk allele (low-risk). Effect modification by HIV suppression status (defined as HIV type 1 RNA level <400 copies/mL for >90% of follow-up time) was evaluated using interaction terms and stratified analyses. **RESULTS:** Of the 333 African American men included in this study, 54 (16%) carried the APOL1 high-risk genotype. Among HIV-infected men with unsuppressed viral loads, those with the high-risk genotype had a 2.42 mL/minute/1.73 m² (95% confidence interval [CI], -3.52 to -1.32) faster annual eGFR decline than men with the low-risk genotype. This association was independent of age, comorbid conditions, baseline eGFR, ancestry, and HIV-related factors. In contrast, the rate of decline was similar by APOL1 genotype among men with sustained viral suppression (-0.16 mL/minute/1.73 m²/year; 95% CI, -.59 to .27; P for interaction <.001). **CONCLUSIONS:** Unsuppressed HIV-infected African Americans with the APOL1 high-risk genotype experience an accelerated rate of kidney function decline; HIV suppression with antiretroviral therapy may reduce these deleterious renal effects.


**BACKGROUND:** Chronic kidney disease (CKD) is a probably underrated public health problem in Sub-Saharan-Africa, in particular in combination with HIV-infection. Knowledge about the CKD prevalence is scarce and in the available literature different methods to classify CKD are used impeding comparison and general prevalence estimates. **METHODS:** This study assessed different serum-creatinine based equations for glomerular filtration rates (eGFR) and compared them to a cystatin C based equation. The study was conducted in Lilongwe, Malawi enrolling a population of 363 adults of which 32% were HIV-positive. **RESULTS:** Comparison of formulae based on Bland-Altman-plots and accuracy revealed best performance for the CKD-EPI equation without the correction factor for black Americans. Analyzing the differences between HIV-positive and -negative individuals CKD-EPI systematically overestimated eGFR in comparison to cystatin C and therefore lead to underestimation of CKD in HIV-positives. **CONCLUSIONS:** Our findings underline the importance for standardization of eGFR calculation in a Sub-Saharan African setting, to further investigate the differences with regard to HIV status and to develop potential correction factors as established for age and sex.


**OBJECTIVES:** Both renal disease and systemic inflammation predict non-AIDS-defining events and overall mortality in HIV-infected patients. Here, we sought to determine the relationships between renal disease and
circulating inflammation markers. METHODS: We performed a secondary analysis of AIDS Clinical Trials Group Study A5224 to determine if markers of renal disease [urine protein:creatinine ratio (uPCR), urine albumin:creatinine ratio (uACR), and estimated glomerular filtration rate (eGFR), using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine and cystatin C-creatinine] were associated with markers of systemic inflammation [high-sensitivity C-reactive protein, interleukin-6, tumour necrosis factor (TNF)-alpha, soluble TNF-alpha receptor I (sTNFRI), sTNFRII, and soluble vascular cellular and intercellular adhesion molecules]. We correlated these renal and inflammatory markers prior to antiretroviral initiation and after 96 weeks of therapy. RESULTS: We found that eGFR (estimated using CKD-EPI cystatin C-creatinine), uPCR, and uACR were significantly correlated with most assessed markers of systemic inflammation prior to antiretroviral initiation. uPCR and eGFR (using CKD-EPI cystatin C-creatinine), but not uACR, remained significantly correlated with most of the assessed inflammatory markers after 96 weeks of antiretroviral therapy (ART). Most of these correlations, although statistically significant, were < 0.50. eGFR using CKD-EPI creatinine was much less frequently associated with inflammation markers and only significantly correlated with sTNFR1 at week 0 and with sTNFRI and II at week 96. CONCLUSIONS: Renal disease and function were associated with systemic inflammation in HIV infection, both before and after ART. Systemic inflammation may partially explain the relationships between proteinuria, albuminuria, and reduced renal function and future adverse outcomes.


BACKGROUND: Data regarding the epidemiology of end-stage renal disease (ESRD) and dialysis in sub-Saharan Africa are scarce and knowledge about the spectrum renal disease is very limited. This study is on the profile of patients with ESRD in a referral hospital in Cameroon. METHODS: Medical records of patients with ESRD covering a 10-year period of activities of the Douala General Hospital were reviewed. Data were retrieved on socio demographic, and clinical data such as major comorbidities, the presumed aetiology of ESRD, blood pressure, biological variables and renal replacement therapy. RESULTS: In all 863 patients were included with 66% being men. Mean age was 47.4 years overall, 48.9 in men and 44.5 in women (p < 0.001). The main background aetiologies of ESRD were hypertension (30.9%), glomerulonephritis (15.8%), diabetes (15.9%), HIV (6.6%) and unknown (14.7%). Participants with HIV, glomerulonephritis or unknown background nephropathy were younger, more likely to be women, to be single and unemployed, while those with hypertension and/or diabetes were older, more likely to be men, to be either married or widow, and to be retired or working in the public sector. A total of 677 patients started haemodialysis with decreasing trend across age quartiles (p = 009), and variation across background nephropathies (p < 0.001). Emergency dialysis unplanned on a temporary catheter occurs in 88.3% of patients. CONCLUSION: This study has revealed substantial gender and age differentials in the socio-demographic features and background nephropathy in patients with ESRD in this setting. The likelihood of starting maintenance dialysis varied across background nephropathies, driven at least in part by age differences across background nephropathies.


BACKGROUND: Chronic kidney disease (CKD) is an important issue for individuals who live with human immunodeficiency virus (HIV) following the use of highly active antiretroviral therapy; however, the prevalence rate of CKD varies between countries. METHODS: The present study screened HIV-infected patients in a medical center and a regional teaching hospital in southern Taiwan from January 2008 to December 2012. CKD was defined as a urine microalbumin-to-creatinine ratio >/=30 mg/g, and/or a protein >/=1 + on urine dipstick examination, and/or an estimated glomerular filtration rate <60 mL/min/1.73 m(2) for 3 months. The prevalence rate and the analyzed
associated factors of CKD were determined. RESULTS: Among 1639 HIV-infected patients, only 512 had adequate data to be enrolled in the study. Thirty-six (7.03%) of these patients had CKD, and 476 did not. In a univariate analysis, CKD was associated with an older age, a higher peak HIV RNA load, diabetes mellitus (DM), hypertension, exposure to antiretroviral therapy, and cholesterol levels $\geq 240$ mg/dL. Multivariate analysis revealed that DM, hypertension, and cholesterol $\geq 240$ mg/dL were statistically significant factors. CONCLUSION: In Taiwan, the prevalence of CKD in HIV-infected patients was low (7.03%). The classical risk factors for CKD, such as DM, hypertension, and hypercholesterolemia, were demonstrated to be associated with CKD in Taiwanese HIV-infected patients.


BACKGROUND: Global glomerulosclerosis is characteristic of chronic kidney disease and also occurs with normal aging. Our goal was to determine the upper limit of normal for number of globally sclerotic glomeruli. METHODS: Core-needle biopsies of the renal cortex were obtained at the time of living kidney transplantation at three centers between 1998 and 2011. The number of globally sclerotic glomeruli was averaged across two biopsy sections. Quantile regression was used to estimate the 95th percentile for globally sclerotic glomeruli as the upper reference limit. There were 2052 donors (mean age 43 years, 41% male, 10% hypertensive), with a mean (SD) of 16.0 (9.7) glomeruli and 0.47 (0.99) globally sclerotic glomeruli on biopsy; only 2.6% had $>5\%$ fibrosis. RESULTS: In a multivariable model excluding hypertensive donors, independent predictors of the number of globally sclerotic glomeruli were age, total number of glomeruli and cortex area. A simplified model was used to estimate the 95th percentile for number of globally sclerotic glomeruli by total number of glomeruli and age. For a biopsy section with 17-32 total glomeruli, the 95th percentile ranged from 1 for a 20-year old to 5.5 for a 70-year old donor. Hypertensive donors were more likely to have an abnormal number of globally sclerotic glomeruli (OR = 1.79, P = 0.035). CONCLUSIONS: We have derived the 95% reference limit for number of globally sclerotic glomeruli in ostensibly healthy individuals accounting for age and the biopsy characteristics. Numbers of globally sclerotic glomeruli in a kidney biopsy that exceed these thresholds suggest chronic pathological injury in excess of that expected with normal aging.


A third of African Americans with sporadic focal segmental glomerulosclerosis (FSGS) or HIV-associated nephropathy (HIVAN) do not carry APOL1 renal risk genotypes. This raises the possibility that other APOL1 variants may contribute to kidney disease. To address this question, we sequenced all APOL1 exons in 1437 Americans of African and European descent, including 464 patients with biopsy-proven FSGS/HIVAN. Testing for association with 33 common and rare variants with FSGS/HIVAN revealed no association independent of strong recessive G1 and G2 effects. Seeking additional variants that might have been under selection by pathogens and could represent candidates for kidney disease risk, we also sequenced an additional 1112 individuals representing 53 global populations. Except for G1 and G2, none of the 7 common codon-altering variants showed evidence of selection or could restore lysis against trypanosomes causing human African trypanosomiasis. Thus, only APOL1 G1 and G2 confer renal risk, and other common and rare APOL1 missense variants, including the archaic G3 haplotype, do not contribute to sporadic FSGS and HIVAN in the US population. Hence, in most potential clinical or screening applications, our study suggests that sequencing APOL1 exons is unlikely to bring additional information compared to genotyping only APOL1 G1 and G2 risk alleles.
BACKGROUND: Among human immunodeficiency virus (HIV)-infected youth, the role of renal disease (RD) and its management has become increasingly important as these children/adolescents mature into young adults. The identification of predictors of abnormal renal laboratory events (RLE) may be helpful in the management of their HIV infection and its associated renal complications. METHODS: Data collected from HIV-infected youth followed for >/= 48 months were analyzed to identify predictors of resolution versus persistence of RLE and determine the utility of RLE to predict the onset of RD. Analysis included descriptive and inferential methods using a multivariable extended Cox proportional hazards model. RESULTS: Of the 1,874 at-risk children enrolled in the study, 428 (23 %) developed RLE, which persisted in 229 of these (54 %). CD4 percentages of <25 % [hazard ratio (HR) 0.63, p < 0.002] and an HIV viral load of >100,000 copies/ml (HR 0.31, p < 0.01) were associated with reduced rates of resolution, while in most cases exposure to highly active antiretroviral therapy (HAART)/nephrotoxic HAART prior to or subsequent to RLE were not. Persistence of RLE was 88 % sensitive for identifying new RD. Negative predictive values for RD were >95 % for both the at-risk cohort and those with RLE. CONCLUSIONS: Advanced HIV disease predicted persistence of RLE in HIV-infected youth. Persistent RLE were useful for identifying RD.


BACKGROUND: Chronic kidney disease (CKD) is a major health issue for HIV-positive individuals, associated with increased morbidity and mortality. Development and implementation of a risk score model for CKD would allow comparison of the risks and benefits of adding potentially nephrotoxic antiretrovirals to a treatment regimen and would identify those at greatest risk of CKD. The aims of this study were to develop a simple, externally validated, and widely applicable long-term risk score model for CKD in HIV-positive individuals that can guide decision making in clinical practice. METHODS AND FINDINGS: A total of 17,954 HIV-positive individuals from the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study with >/=3 estimated glomerular filtration rate (eGFR) values after 1 January 2004 were included. Baseline was defined as the first eGFR > 60 ml/min/1.73 m2 after 1 January 2004; individuals with exposure to tenofovir, atazanavir, atazanavir ritonavir, lopinavir ritonavir, other boosted protease inhibitors before baseline were excluded. CKD was defined as confirmed (>3 mo apart) eGFR </= 60 ml/min/1.73 m2. Poisson regression was used to develop a risk score, externally validated on two independent cohorts. In the D:A:D study, 641 individuals developed CKD during 103,185 person-years of follow-up (PYFU; incidence 6.2/1,000 PYFU, 95% CI 5.7-6.7; median follow-up 6.1 y, range 0.3-9.1 y). Older age, intravenous drug use, hepatitis C coinfection, lower baseline eGFR, female gender, lower CD4 count nadir, hypertension, diabetes, and cardiovascular disease (CVD) predicted CKD. The adjusted incidence rate ratios of these nine categorical variables were scaled and summed to create the risk score. The median risk score at baseline was -2 (interquartile range -4 to 2). There was a 1:393 chance of developing CKD in the next 5 y in the low risk group (risk score < 0, 33 events), rising to 1:47 and 1:6 in the medium (risk score 0-4, 103 events) and high risk groups (risk score >/= 5, 505 events), respectively. Number needed to harm (NNTH) at 5 y when starting unboosted atazanavir or lopinavir ritonavir among those with a low risk score was 1,702 (95% CI 1,166-3,367); NNTH was 202 (95% CI 159-278) and 21 (95% CI 19-23), respectively, for those with a medium and high risk score. NNTH was 739 (95% CI 506-1462), 88 (95% CI 69-121), and 9 (95% CI 8-10) for those with a low, medium, and high risk score, respectively, starting tenofovir, atazanavir ritonavir, or another boosted protease inhibitor. The Royal Free Hospital Clinic Cohort included 2,548 individuals, of whom 94 individuals developed CKD (3.7%) during 18,376 PYFU (median follow-up 7.4 y, range 0.3-12.7 y). Of 2,013 individuals included from the SMART/ESPRIT control arms, 32 individuals developed CKD (1.6%) during 8,452 PYFU (median follow-up 4.1 y, range 0.6-8.1 y). External validation showed that the risk score predicted well in these cohorts. Limitations of this study included limited data on race and no information on proteinuria. CONCLUSIONS: Both traditional and HIV-related risk
factors were predictive of CKD. These factors were used to develop a risk score for CKD in HIV infection, externally validated, that has direct clinical relevance for patients and clinicians to weigh the benefits of certain antiretrovirals against the risk of CKD and to identify those at greatest risk of CKD.


BACKGROUND: The outcome of kidney transplantation in human immunodeficiency virus (HIV)-positive patients who receive organs from HIV-negative donors has been reported to be similar to the outcome in HIV-negative recipients. We report the outcomes at 3 to 5 years in HIV-positive patients who received kidneys from HIV-positive deceased donors. METHODS: We conducted a prospective, nonrandomized study of kidney transplantation in HIV-infected patients who had a CD4 T-cell count of 200 per cubic millimeter or higher and an undetectable plasma HIV RNA level. All the patients were receiving antiretroviral therapy (ART). The patients received kidneys from deceased donors who tested positive for HIV with the use of fourth-generation enzyme-linked immunosorbent assay at the time of referral. All the donors either had received no ART previously or had received only first-line ART. RESULTS: From September 2008 through February 2014, a total of 27 HIV-positive patients underwent kidney transplantation. Survivors were followed for a median of 2.4 years. The rate of survival among the patients was 84% at 1 year, 84% at 3 years, and 74% at 5 years. The corresponding rates of graft survival were 93%, 84%, and 84%. (If a patient died with a functioning graft, the calculation was performed as if the graft had survived.) Rejection rates were 8% at 1 year and 22% at 3 years. HIV infection remained well controlled, with undetectable virus in blood after the transplantation. CONCLUSIONS: Kidney transplantation from an HIV-positive donor appears to be an additional treatment option for HIV-infected patients requiring renal-replacement therapy. (Funded by Sanofi South Africa and the Roche Organ Transplantation Research Foundation.).


OBJECTIVES: Our aim is to describe the impact of emtricitabine (FTC)/tenofovir (TDF) versus other nucleoside reverse transcriptase inhibitor (NRTIs)-based regimens on renal function of human immunodeficiency virus (HIV) naive patients >50 years old who started combination antiretroviral therapy (cART). DESIGN: National, retrospective cohort analysis of patients >50 years old when they started cART (January 1, 2006-December 31, 2009). METHODS: We compared renal safety (changes in estimated glomerular filtration rate [eGFR] during the first year, and time to renal events during 4 years of follow-up) in FTC/TDF versus non-FTC/TDF users. Among FTC/TDF users, we compared protease inhibitors vs non-nucleoside reverse transcriptase inhibitors and Lopinavir/ritonavir vs Efavirenz. RESULTS: We included 103 patients: median age: 54.9 years, 84% males, median CD4 count 247 cells/mul, median viral load 4.7 log; median follow up 18 months (max: 48 months); 73 started with FTC/TDF and 30 with other NRTIs. Change in eGFR was significantly worse for ritonavir-boosted lopinavir (LPV/r) vs efavirenz (EFV) users in the FTC/TDF group (71.2 vs 98.9 ml/min/1.73 m(2) at month 12, P < 0.05). The risk of renal events (progression to an Chronic Kidney Disease Epidemiology Collaboration value < 60 ml/min/1.73 m(2) in subjects with baseline values >60) was comparable for FTC/TDF users and non users, but was higher and almost significant for LPV/r as compared to EFV users in the FTC/TDF group (adjusted hazard ratio 6.1, 95% CI 0.8-45.5). CONCLUSIONS: In our study with a population of HIV infected subjects >/= 50 years old, renal safety was similar for FTC/TDF and other NRTI-based regimens, but worse for LPV/r as compared to other regimens.

BACKGROUND: Chronic kidney disease (CKD) is an important comorbidity during human immunodeficiency virus (HIV) infection. Historically, HIV-associated nephropathy has been the predominant cause of CKD and has primarily been observed in people of African ancestry. This study aims to investigate the role of ethnicity in relation to CKD risk in recent years. METHODS: Analyses were performed including 16 836 patients from the Dutch AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort. Baseline was defined as the first available creatinine level measurement after 1 January 2007; CKD was defined as a glomerular filtration rate of <60 mL/min/1.73 m². The associations between ethnicity and both prevalent CKD at baseline and incident CKD during follow-up were analyzed. RESULTS: The prevalence of baseline CKD was 2.7% (460 of 16 836 patients). Birth in a sub-Saharan African country (hereafter, "SSA origin") was significantly associated with baseline CKD (adjusted odds ratio 1.49; 95% confidence interval [CI], 1.04-2.13). During follow-up (median duration, 4.7 years; interquartile range, 2.4-5.2), the rate of newly developing CKD was similar between patients of SSA origin and those born in Western Europe, Australia, or New Zealand (adjusted hazard ratio, 1.00; 95% CI, .63-1.59). CONCLUSIONS: Among HIV-infected patients in the Netherlands, being of SSA origin was associated with a higher baseline CKD prevalence but had no impact on newly developing CKD over time. This suggests a shift in the etiology of CKD from HIV-associated nephropathy toward other etiologies.


INTRODUCTION: Several studies have demonstrated that renal transplantation in HIV positive patients is both safe and effective. However, none of these studies have specifically examined outcomes in patients with HIV-associated nephropathy (HIVAN). METHODS: Medical records of all HIV-infected patients who underwent kidney transplantation at Johns Hopkins Hospital between September 2006 and January 2014 were reviewed. Data was collected to examine baseline characteristics and outcomes of transplant recipients with HIVAN defined pathologically as collapsing focal segmental glomerulosclerosis (FSGS) with tubulo-interstitial disease. RESULTS AND DISCUSSION: During the study period, a total of 16 patients with HIV infection underwent renal transplantation. Of those, 11 patients were identified to have biopsy-proven HIVAN as the primary cause of their end stage renal disease (ESRD) and were included in this study. They were predominantly African American males with a mean age of 47.6 years. Seven (64%) patients developed delayed graft function (DGF), and 6 (54%) patients required post-operative dialysis within one week of transplant. Graft survival rates at 1 and 3 years were 100% and 81%, respectively. Acute rejection rates at 1 and 3 years were 18% and 27%, respectively. During a mean follow up of 3.4 years, one patient died. CONCLUSIONS: Acute rejection rates in HIVAN patients in this study are higher than reported in the general ESRD population, which is similar to findings from prior studies of patients with HIV infection and ESRD of various causes. The high rejection rates appear to have no impact on short or intermediate term graft survival.


HIV-positive patients are at increased risk of developing chronic kidney disease. Although guidelines recommend regular monitoring of renal function in individuals living with HIV, the optimal frequency remains to be defined. In this review, we discuss the renal syndromes that may be identified at an earlier stage via routine
assessment of kidney function, and provide guidance in terms of the frequency of monitoring, the most useful tests to perform, and their clinical significance. Specifically, we address whether annual monitoring of kidney function is appropriate for the majority of HIV-positive patients.


AIM: To identify the prevalence and predictors of abnormal renal function among HIV-positive Chinese patients prior to antiretroviral therapy (ART) initiation and to evaluate subsequent changes in renal function after ART exposure. METHODS: We conducted a nationwide cohort study of subjects who enrolled in the national Chinese ART program from January 1, 2012 to December 31, 2012. We estimated the glomerular filtration rate (eGFR) of subjects prior to and after initiating ART. Risk factors for abnormal renal function, as defined by eGFR <60 ml/min/1.73m2, at baseline and follow-up were assessed by logistic regression and Cox proportional hazards regression models, respectively. RESULTS: Among 41,862 subjects, at ART baseline, 3.3% had a baseline eGFR <60 ml/min/1.73m2 and 24.2% had eGFR = 60-90 ml/min/1.73m2. Adjusted baseline risk factors for baseline eGFR <60 ml/min/1.73m2 were older age (Adjusted odds ratio [AOR] = 5.19, 95% confidence interval [CI]: 4.52-5.67), female (AOR = 1.68, 95% CI: 1.47-1.93), hemoglobin <120g/L (AOR = 1.68, 95% CI: 1.47-1.93), blood glucose >6.1 mmol/L (AOR = 1.46, 95% CI: 1.25-1.72), and hepatitis C co-infection (AOR = 1.36, 95% CI: 1.06-1.73). Among subjects with baseline eGFR >90 ml/min/1.73m2, the incidence of the eGFR falling to <60 ml/min/1.73m2 was 0.92/100 person-years after a median of 15.0 months of ART. Being on a tenofovir with lopinavir/ritonavir regimen (Adjusted hazard ratio [AHR] = 3.02, 95% CI: 1.96-4.66) and having an unsuppressed viral load (AHR = 2.70, 95% CI: 1.80-4.03) were independent predictors for eGFR <60 ml/min/1.73m2 after ART initiation as well as older age, female, and hemoglobin <120 g/L.

CONCLUSION: A high proportion of HIV-positive subjects in China presented with abnormal renal function prior to ART initiation. But the incidence of the eGFR decrease after ART was low. Patient renal function should be regularly monitored by eGFR before initiating and during ART.

Prevention


This article reports on older adults' perceptions and opinions about the importance of HIV/AIDS prevention education and reasons for participation. It reports on specific themes that emerged from five focus groups consisting of 52 ethnically diverse adults 50 years and older. Participants identified four themes regarding HIV/AIDS prevention education: 1) “Knowing someone who has it”, 2) “Tell me about it at work”, 3) “We’re not dead yet”, and 4) “How do I talk about this with my doctor?” The article discusses the meaning of the findings as they relate to current knowledge about HIV prevention education and older adults, sexual activity, and implications for social work research, education, and outreach.


AIM: The transgender community has long been marginalized in society. As the world's population ages, gender-unbiased health services for this growing population, with age-related chronic illnesses, will be essential. To optimally eliminate hurdles that trans individuals often confront when requesting services, it appears judicious to eliminate the strict and antiquated definition of what constitutes "normal" female and "normal" male. METHODS: A
A review of literature on transgender medicine on PubMed over the last five years was conducted. RESULTS: Existing statistics indicate that unacceptable bias and discrimination are occurring, making trans patients less likely to seek care. There are emerging initiatives that address the transgender and gender non-conforming population. Ongoing needs include defining what constitutes "gender equal," understanding the continuum of gender identity, and establishing and implementing guidelines for gender equal counseling and care. CONCLUSIONS: With the routine practice of defining sex at birth and equating sex with gender in the health care setting, the transgender patient encounters multiple barriers to accessing and acquiring health care services. These strict gender labels appear to preclude the institution of gender equal care. Care templates on gender equal patient encounters should be implemented to better address transgender health needs in a non-biased manner.


The immune systems of men and women differ in significant ways, especially after puberty. In particular, females are generally more prone to autoimmunity, but experience lower rates of infections and chronic inflammatory disease. Sex hormones, genes encoded on the sex chromosomes, and gender-specific behaviors likely contribute to these differences. The aging process is associated with changes in the composition and function of the immune system and these changes may occur at an accelerated rate in men as compared to women. Moreover, after the age of menopause, the incidence of chronic inflammatory disease in women approaches or exceeds that observed in males. At the same time, the incidence of autoimmunity in post-menopausal women is decreased or equivalent to the rates observed in similarly-aged men. Additional studies addressing the influence of sex on the pathogenesis of chronic and autoimmune diseases in the aged are warranted.


OBJECTIVE: To know the vulnerability of the elderly to the HIV infection in the context of preventive practices. METHOD: Exploratory qualitative study, lead from December 2012 to May 2013, with 37 nursing Coexistence Groups in Joao Pessoa - Paraiba. The Focus Group was elected as the research technique, and the empirical material obtained was subjected to a Content Analysis Technique, thematic modality. RESULTS: The elderly recognize the importance of preventive practices, but they face difficulties in its use when their emotional relationships with their partners do not favor preventive behavior, resulting in vulnerability. The elderly showed the population groups most vulnerable to HIV and do not recognize themselves as such. CONCLUSION: The complexity of the various contexts experienced by the elders of this study indicate the need for more research that allows advances in the understanding of subjectivity imposed in relations that underlie the aging process and the experience of sexuality in this age group.


Background: There are increasing reports of sexual transmission of hepatitis C virus (HCV) among HIV-positive men who have sex with men (MSM). Still unclear is the level of HCV knowledge and the risk factors specific to HCV transmission among this population. This study compared HCV knowledge and risk practices among HIV-positive, HIV-negative and HIV-untested gay and bisexual men in Australia. Methods: Participants (n = 534) completed an online survey assessing sexual risk practices, HCV knowledge, perceived risk of acquiring HCV and perceptions of people with HCV and who inject drugs. Results: HIV-positive participants were older, reported greater engagement in sexual risk and injecting drug practices, felt they were at greater risk of acquiring HCV, were less likely to socially and sexually
exclude people with HCV and had more positive attitudes towards people who inject drugs and people with HCV compared with HIV-negative and HIV-untested participants. HIV-untested participants were younger, reported fewer HCV-related serosorting practices and were more likely to socially and sexually exclude people with HCV than the other groups. Conclusions: Findings suggest that HCV education and prevention for gay men may be most effective if tailored according to HIV status. For HIV-positive men, health promotion could focus on specific sexual practices and biological factors linked to HCV transmission, regular HCV testing and better strategies for disclosure of HCV serostatus. For HIV-negative and HIV-untested men, there should be a more general focus on awareness, changing attitudes towards HCV testing and increasing general knowledge around HCV, including evidence of sexual transmission.


It is widely known that older women are at lesser risk for sexual violence than younger women, but current inattention to older women in the gender-based violence (GBV) field has minimized the experiences of older women survivors at great detriment to their health and rights. For example, health providers seldom ask older women about their sexual activity and relationships, a neglect that leads to older women being excluded from necessary HIV testing and care as well as support services for abuse. This oversight is increasingly worrisome given the rise in new HIV infections among adults age 50 and older in recent years, with the majority of transmissions stemming from individuals unaware of their HIV-positive status. Building on sexual rights scholarship, this paper argues for an approach to public health interventions for GBV and HIV that acknowledges older women - their sexuality, sexual agency, and activity - so that health providers and advocates acknowledge and serve older survivors.


PURPOSE: To explore primary care providers' HIV prevention practices for older adults. Primary care providers' perceptions and awareness were explored to understand factors that affect their provision of HIV prevention materials and HIV screening for older adults. DESIGN AND METHOD: Data were collected through 24 semistructured interviews with primary care providers (i.e., physicians, physician assistants, and nurse practitioners) who see patients older than 50 years. RESULTS: Results reveal facilitators and barriers of HIV prevention for older adults among primary care providers and understanding of providers' HIV prevention practices and behaviors. Individual, patient, institutional, and societal factors influenced HIV prevention practices among participants, for example, provider training and work experience, lack of time, discomfort in discussing HIV/AIDS with older adults, stigma, and ageism were contributing factors. Furthermore, factors specific to primary and secondary HIV prevention were identified, for instance, the presence of sexually transmitted infections influenced providers' secondary prevention practices. IMPLICATIONS: HIV disease, while preventable, is increasing among older adults. These findings inform future research and interventions aimed at increasing HIV prevention practices in primary care settings for patients older than 50.


Background: There is a lack of research that examines event-level lubricant use and outcomes among gay and bisexual men, with the majority of current research addressing lubricant use within the context of sexual risk. Most studies examining sexual health among gay and bisexual men have relied on convenience sampling strategies for
participant recruitment. Methods: Data were collected from the 2012 wave of the National Survey of Sexual Health and Behaviour (NSSHB), which involved the administration of an online questionnaire to a nationally representative probability sample of women and men in the United States aged 18 years and older, including an oversampling of self-identified gay and bisexual men and women. The findings from gay (n = 307) and bisexual (n = 25) participants who reported sexual behaviours with other male partners during their last sexual encounter are included in this paper. Post-stratification data weights were applied to the data to maximise the generalisability of the findings. Results: Men who reported lubricant use during their last sexual event with a male partner (n = 163) were significantly more likely to be non-White, Hispanic and between 30 and 39 years old. Bisexual men had lower odds of using lubricant than gay-identified men. The majority of men reported using lubricant during anal intercourse, along with lower numbers with a range of other sexual behaviours. Conclusion: Public health promotion specialists should consider recommending continued lubricant use as a part of comprehensive sexual health promotion efforts for gay and bisexual men, including that it reduces pain and maximises pleasure.


The use of cognitive-behavioral interventions that aim to improve men's health-seeking behaviors via women—a trend that grows increasingly troublesome as gender inequality persists—cannot address the deep-seated social, economic, and political inequalities contributing to the spread of HIV/AIDS, such as sexism and poverty. Such methods often rely on generalizations about men and women and regard female empowerment as a key goal, despite employing shaky definitions of the concept. Here we use the principles of health promotion, particularly determinants of health, to reflect upon and critique current interventions and present alternative programming models that engage both men and women in changing men's health-seeking behaviors and working "upstream" rather than "downstream" of the epidemic.


BACKGROUND: This study aims to report on a newly developed Safer Indoor Work Environmental Scale that characterises the social, policy and physical features of indoor venues and social cohesion; and using this scale, longitudinally evaluate the association between these features on sex workers' (SWs') condom use for pregnancy prevention. METHODS: Drawing on a prospective open cohort of female SWs working in indoor venues, a newly developed Safer Indoor Work Environment Scale was used to build six multivariable models with generalised estimating equations (GEE), to determine the independent effects of social, policy and physical venue-based features and social cohesion on condom use. RESULTS: Of 588 indoor SWs, 63.6% used condoms for pregnancy prevention in the last month. In multivariable GEE analysis, the following venue-based features were significantly correlated with barrier contraceptive use for pregnancy prevention: managerial practices and venue safety policies (adjusted OR (AOR)=1.09; 95% CI 1.01 to 1.17), access to sexual and reproductive health services/supplies (AOR=1.10; 95% CI 1.01 to 1.20), access to drug harm reduction (AOR=1.13; 95% CI 1.01 to 1.28) and social cohesion among workers (AOR=1.05; 95% CI 1.03 to 1.07). Access to security features was marginally associated with condom use (AOR=1.13; 95% CI 0.99 to 1.29). CONCLUSIONS: The findings of the current study highlight how work environment and social cohesion among SWs are related to improved condom use. Given global calls for the decriminalisation of sex work, and potential legislative reforms in Canada, this study points to the critical need for new institutional arrangements (eg, legal and regulatory frameworks; labour standards) to support safer sex workplaces.

A documentary film on HIV was developed based on social cognitive theory and entertainment educational methods in an effort to increase awareness and encourage protective behavior change related to HIV among older adults. The documentary includes perspectives from racial- or ethnic-minority older adults who are living with HIV and those of health care providers, and was screened in several venues. Authors of this article conducted thematic content analysis of anonymous, written, open-ended responses from 341 film viewers (clinicians and laypeople) who described what they learned about HIV after viewing the film. Four key themes emerged from the analysis: (1) increased awareness about the epidemiology of HIV among older, minority groups and about sexuality among older people; (2) improved general HIV knowledge, including risk reduction strategies and details about HIV testing; (3) awareness of lack of sexual health education among health care providers, and that a call to action is needed; and (4) awareness that HIV reinfection can occur in certain circumstances with people who are already infected. Findings suggest that an educational documentary can be used to effectively increase awareness and knowledge about the impact of HIV among minority older adults, and may also encourage HIV prevention action steps by providers.


This study investigates how internalized sexual minority stigma and enacted sexual minority stigma in health care settings are associated with sexual health risk behaviors (SRBs) and the mediating role of infrequent routine health care and perceived stress among older gay and bisexual (G/B) men living with HIV disease. Survey responses from 135 sexually active older G/B men living with HIV were analyzed using hierarchical linear regression models. Results indicate that one fifth of G/B older adult men living with HIV are engaged in multiple SRBs. Internalized sexual minority stigma and enacted sexual minority stigma in health care settings are significantly associated with SRBs. The relationship between internalized sexual minority stigma and SRBs are mediated by infrequent routine health care and elevated levels of perceived stress. Improved primary and secondary prevention strategies are needed for the growing number of sexually active older G/B men.


In response to the call to create an AIDS Education and Training Center for Nurse Practitioner Education by the Health Resources and Services Administration, The Johns Hopkins University School of Nursing embarked on a transformative curriculum overhaul to integrate HIV prevention, treatment, and care into the Adult/Geriatric Nurse Practitioner Program. A six-step process outlined in the Curriculum Development for Medical Education was followed. A pilot cohort of Adult/Geriatric Nurse Practitioner students were enrolled, including 50% primary care setting and 50% HIV-focused primary care through a 12-month HIV continuity clinic experience. Through this pilot, substantive changes to the program were adopted. Programmatic outcomes were not compromised with the modification in clinical hours. The model of a 12-month HIV continuity clinic experience reduced the number of required preceptors. This model has important implications for the HIV workforce by demonstrating successful integration of HIV and primary care training for nurse practitioners.


BACKGROUND: Although routine human immune deficiency virus (HIV) testing during health care visits is recommended for most adults, many older adults (i.e., ages 50-64 years) do not receive it. This study identified factors associated with HIV testing in the past 12 months (i.e., recent HIV testing) among US adults in the 3 categories of older adulthood (50-54, 55-59, and 60-64 years) for which routine HIV testing is recommended. METHOD: This was a cross-sectional analysis of data from US older adult respondents to the 2010 Behavioral Risk Factor Surveillance System. We calculated prevalence (proportions) of HIV testing by age category and race/ethnicity. Using multiple logistic regression, we identified predisposing, enabling, and need factors associated with recent HIV testing within and across age categories, by race/ethnicity and controlling for covariates. RESULTS: HIV testing prevalence was low (<5%), varied by race/ethnicity, and decreased with age. Within and across age categories, the odds of testing were highest among blacks (odds ratio [OR], 3.47; 95% confidence interval [CI], 2.82-4.25) and higher among Latinos (OR, 2.06; 95% CI, 1.50-2.84) and the oldest and youngest categories of American Indians/Alaska Natives (OR, 2.48; 95% CI, 1.11-5.55; OR, 2.98; 95% CI, 1.49-5.95) than among whites. Those reporting a recent doctor visit (OR, 2.32; 95% CI, 1.92-2.74) or HIV risk behaviors (OR, 3.50; 95% CI, 2.67-4.59) had higher odds of HIV testing. CONCLUSION: Regardless of risk, the oldest older adults, whites, and older women may forego HIV testing. Doctor visits may facilitate HIV testing. Additional research is needed to understand why eligible older adults seen by providers may not be screened for HIV infection.


The Centers for Disease Control and Prevention recommends routine human immunodeficiency virus (HIV) testing of every client presenting for services in venues where HIV prevalence is high. Because older adults (aged >/=50 years) have particularly poor prognosis if they receive their diagnosis late in the course of HIV disease, any screening provided to younger adults in these venues should also be provided to older adults. We examined aging-related disparities in recent (past 12 months) and ever HIV testing in a probability sample of at-risk adults (N = 1238) seeking services in needle exchange sites, sexually transmitted disease clinics, and Latino community clinics that provide HIV testing. Using multiple logistic regression with generalized estimating equations, we estimated associations between age category (<50 years vs. >/=50 years) and each HIV testing outcome. Even after controlling for covariates such as recent injection drug use, older adults had 40% lower odds than younger adults did of having tested in the past 12 months (odds ratio [OR] = 0.6; 95% confidence interval [CI] = 0.40-0.90) or ever (OR = 0.6; 95% CI = 0.40-0.90). Aging-related disparities in HIV testing exist among clients of these high HIV prevalence venues and may contribute to known aging-related disparities in late diagnosis of HIV infection and poor long-term prognosis.


African Americans are disproportionately affected by HIV/AIDS, but little is known about the risky sexual behaviors of older African Americans. This cross-sectional, comparative, and descriptive study investigated the self-reported sexual behaviors of sexually active older African Americans. The nonrandom sample (N = 78) included single
African American men (59%) and women (41%), 50-74 years of age. Participants were recruited from various community sites, and data were collected with a standard sexual history questionnaire. Participants reported practicing risky behaviors such having unprotected oral, anal, and vaginal sex (96.5%), and having multiple sex partners (37.2%). There were several significant gender differences such as males using condoms more for vaginal sexual activity, and they discussed using a condom more than females. Faced with an aging population and a growing incidence of HIV/AIDS, older adults need to know the types of sexual behaviors that put them at risk and skills to reduce risky behaviors. Age/gender-appropriate interventions for HIV prevention are needed for older African Americans.


BACKGROUND: Older adults are remaining sexually active for longer periods of time, underscoring the need to assess sexual activity patterns in this group and identify differences by race/ethnicity, some of which may have implications for the development and implementation of sexual risk reduction interventions. METHODS: Using data from the 2010 National Social Life, Health, and Aging Project, this study examined responses from 1,429 adults aged 60 years and older. Multinomial logistic regression compared sexual behaviors, health-related indicators, interactions with healthcare professionals, and HIV-related perceptions across participants’ race/ethnicity. RESULTS: Approximately 81% of participants self-reported as non-Hispanic white, 10.59% as African American, and 8.05% as Hispanic. On average, participants were 69.9 years of age. In the previous year, 49.3% of participants engaged in sexual intercourse; only 3% used condoms. The majority of participants (83.1%) visited a physician at least twice in the previous year, 30.9% had discussed sex with a physician since turning 50, and 14.2% had been tested for HIV. Relative to non-Hispanic whites, African Americans were more likely to be divorced (OR=3.23, P<0.001) or widowed (OR=2.90, P<0.001); have more lifetime sexually transmitted infection (STI) diagnoses (OR=1.67, P=0.030); and have paid for sex (OR=2.83, P=0.002). Although African Americans had greater perceived risk for HIV infection (OR=1.66, P=0.046), they were less likely to have discussed sex with a physician since turning 50 (OR=0.45, P=0.009).

CONCLUSION: Contextualized interventions to improve patient-provider communication and proactive screening behaviors in sexually-active and aging African Americans are needed.


Background: With society ageing, sexually transmissible infections (STIs) in the older population are of interest from an economic, health-related and social burden perspective. Few studies on STIs in men older than 60 years of age exist. Methods: A retrospective study was performed looking at characteristics of, and STIs in, 29 106 men (of which 689 were older than 60 years of age), at first presentation, visiting the only South Australian public sexually transmitted diseases (STD) clinic over a 13-year period. Results: Older men [men who have sex with men (MSM) and men who have sex with women (MSW)] were less likely than younger men to have been tested for HIV. Conclusion: There is a need for increased HIV testing in older men.


Little is known about the impact of HIV and aging on cognitive functioning. This New York City cross-sectional study of aging HIV-positive gay and bisexual men assessed their neuropsychological state. Working memory and verbal abstract reasoning were relatively intact. After 55 years of age, attention abilities were impaired. Executive function impairment was present regardless of age and education. Results suggest the need for HIV-specific norms, and the use of neuropsychological assessments (i.e. baseline and over time) as a cost-effective way to assess HIV-related cognitive decline in developed and under-developed countries.


OBJECTIVE: To assess the correlates for bisexual behaviors, HIV knowledge, and HIV/AIDS-related stigmatizing/discriminatory attitudes among men who have sex with men (MSM). METHODS: A cross-sectional survey among MSM was conducted in 2011 to provide demographics, sexual behaviors, HIV knowledge, HIV/AIDS-related stigmatizing/discriminatory attitudes, and services in Jinan, Qingdao, and Yantai of Shandong Province of China. RESULTS: Of 1230 participants, 82.8% were single, 85.7% aged <35 years, and 47.2% received college or higher education. There were 28.6% MSM who reported to be married or cohabitating or ever had sex with woman in the past 6 months (P6M). 74.5% had >/=6 HIV-related knowledge score. The average total score of stigmatizing/discriminatory attitude was 37.4+/4.4(std deviation). Bisexual behavior was independently associated with higher levels of HIV/AIDS-related stigma/discrimination(AOR = 1.1, 95% CI:1.0-1.1), older age(AOR = 1.2, 95%CI:1.1-1.2), and lower HIV-related knowledge score(AOR = 1.6, 95%CI:1.2-2.2). HIV knowledge score >/=6 was independently associated with lower levels of HIV/AIDS-related stigma/discrimination(AOR = 1.3, 95%CI:1.2-1.3), less bisexual behaviors(AOR = 0.6, 95%CI:0.5-0.9), ever received a test for HIV in the past 12 months (P12M)(AOR = 3.2, 95%CI:2.3-4.5), college or higher level education(AOR = 1.9, 95%CI:1.4-2.6), consistent condom use with men in P6M(AOR=6.9, 95%CI:4.6-10.6), recruited from internet or HIV testing sites(AOR = 11.2, 95%CI:8.0-16.1) and bars, night clubs, or tea houses(AOR = 2.5, 95%CI:1.7-4.8). Expressing higher levels of HIV/AIDS-related stigmatizing/discriminatory attitudes was independently associated with bisexual behaviors(\(abeta = 0.9, 95%\)CI:0.4-1.4), lower HIV-related knowledge score(\(abeta = 3.6, 95%\)CI:3.0-4.1), the number of male sex partners in the past week >/=2(\(abeta = 1.4, 95%\)CI:1.0-1.9), unprotected male anal sex in P6M(\(abeta = 1.0, 95%\)CI:0.5-1.6), and inversely associated with ever received HIV test(\(abeta = 1.4, 95%\)CI:0.8-2.0) and peer education in P12M(\(abeta = 1.4, 95%\)CI:0.9-1.9). CONCLUSION: HIV/AIDS-related stigmatizing/discriminatory attitudes were associated with bisexual behaviors, low HIV testing rate, lower HIV-related knowledge and risk behaviors. This study called for innovative programs that would reduce HIV/AIDS-related stigmatizing/discriminatory attitudes and bisexual behaviors and improve the uptake of prevention service among MSM.


By 2015, one-half of all HIV-positive persons in the U.S. will be 50-plus years of age, and as many as 30 % of older adults living with HIV/AIDS continue to engage in unprotected sexual intercourse. Contemporary positive prevention models often include mental health treatment as a key component of HIV prevention interventions. This secondary data analysis characterized longitudinal patterns of sexual behavior in HIV-positive older adults enrolled in a randomized controlled trial of group mental health interventions and assessed the efficacy of psychosocial
treatments that targeted depression to reduce sexual risk behavior. Participants were 295 HIV-positive adults ≥50 years of age experiencing mild to severe depressive symptoms, randomized to one of three study conditions: a 12-session coping improvement group intervention, a 12-session interpersonal support group intervention, or individual therapy upon request. Approximately one-fifth of participants reported one or more occasions of unprotected anal or vaginal intercourse with HIV-negative sexual partners or persons of unknown HIV serostatus over the study period. Changes in sexual behavior did not vary by intervention condition, indicating that standalone treatments that target and reduce depression may be insufficient to reduce sexual risk behavior in depressed HIV-positive older adults.


This systematic review collates, examines and synthesizes condom use interventions for middle-aged and older adults. Associations between effectiveness and theoretical basis, behaviour change techniques, mode of delivery and treatment fidelity were explored. Five interventions were included; one was effective. Compared to interventions with non-significant findings, the effective telephone-administered intervention used theory to a greater extent, had a higher number of behaviour change techniques and employed more treatment fidelity strategies. There is a need to develop theory-based interventions targeting condom use among this population and evaluate these in randomised controlled trials that are rigorously designed and reported. Health psychologists have a key role in this endeavour.


Antiretroviral preexposure prophylaxis has huge potential for reducing the rates of new HIV infections in at risk populations. Oral and vaginal antiretroviral formulations have been evaluated in multiple Phase IIB and Phase III effectiveness trials and there is clear evidence that these products work when used. The converse is also true; antiretrovirals do not work when they are not used and unfortunately adherence is a problem for both HIV treatment and prevention. As a consequence, long-acting injectable and implantable antiretroviral formulations are being developed for the treatment and prevention of HIV infection. It is hoped they will reduce the burden of product adherence associated with the use of oral and topical products and improve clinical outcomes associated with their use. The purpose of this review is to summarize recent preclinical and clinical research in this area of HIV prevention.


Data from a social network-based human immunodeficiency virus (HIV)/sexually transmitted infection (STI) prevention study with a total of 330 men and women at high risk for HIV/STIs were used to examine the relationships between substance use, depressive symptoms, general health, cardiovascular disease risk factors, sociodemographic characteristics, and systolic/diastolic blood pressure (SBP/DBP). Approximately 60% of the participants had prehypertension to stage 2 hypertension. In the base model, older patients (P<.0001), men (P=.003), and patients with poorer self-reported health (P=.029) were significantly associated with high SBP, whereas older age (P<.001) and higher body mass index (P<.001) were significantly associated with higher DBP. After adjusting for the base model, high frequency of alcohol drinking and high frequency of binge drinking remained significant for high SBP and DBP. These data suggest that future cardiovascular disease programs should target moderate alcohol consumption to improve blood pressure among individuals at high risk for HIV/STIs.

Sexual behavior among older adults with HIV in Sub-Saharan Africa has been understudied despite the burgeoning of this population. We examined sexual behavior among older adults living with HIV in Uganda. Participants were eligible for the study if they were 50 years of age or older and living with HIV. Quantitative data were collected through face-to-face interviews, including demographic characteristics, health, sexual behavior and function, and mental health. Of respondents, 42 were men and 59 women. More than one-quarter of these HIV-positive older adults were sexually active. A greater proportion of older HIV-positive men reported being sexually active compared to women (54 vs. 15 %). Among those who are sexually active, a majority never use condoms. Sixty-one percent of men regarded sex as at least somewhat important (42 %), while few women shared this opinion (20 %). Multivariate logistic regression analyses revealed that odds of sexual activity in the past year were significantly increased by the availability of a partner (married/cohabitating), better physical functioning, and male gender. As more adults live longer with HIV, it is critical to understand their sexual behavior and related psychosocial variables in order to improve prevention efforts.


PURPOSE OF THE STUDY: Aging and HIV/AIDS research focuses primarily on standardized clinical, social, and behavioral measures, leaving unanswered questions about how this chronic and stigmatizing condition affects life course expectations and the meaning of aging with the disease. Utilizing Gaylene Becker's (1997) life course disruption theory, we explored older African Americans' experiences of living with HIV/AIDS. DESIGN AND METHODS: A purposive sample (N = 43) of seropositive African Americans aged 50 and older was selected from a parent study. Thirteen participants completed one semi-structured in-depth interview on life course expectations and experiences of living with HIV/AIDS. Interview transcripts were analyzed using standard qualitative coding and thematic analysis. RESULTS: Responding to broad, open-ended questions about the impact of HIV on life course expectations, participants emphasized how HIV limited their ability to experience sexuality and intimacy. Two major themes emerged, damaged sexuality and constrained intimacy. IMPLICATIONS: Older African Americans' discussions of living with HIV focused on the importance of and the challenges to sexuality and intimacy. Researchers and clinicians should be attentive to significant and ongoing HIV-related challenges to sexuality and intimacy facing older African Americans living with HIV/AIDS.


In the last four decades, we have witnessed vast and important transitions in the social, economic, political, and health contexts of the lived experiences of gay men in the United States. This dynamic period, as evidenced most prominently by the transition of the gay rights movement to a civil rights movement, has shifted the exploration of gay men's health from one focusing primarily on HIV/AIDS into a mainstream consideration of the overall health and wellbeing of gay men. Against this backdrop, aging gay men in the United States constitute a growing population, for whom further investigations of health states and health-related disparities are warranted. In order to advance our understanding of the health and wellbeing of aging gay men, we outline here a multilevel, ecodesign conceptual framework that integrates salient environmental, social, psychosocial, and sociodemographic factors into sets of macro-, meso-, and micro-level constructs that can be applied to comprehensively study health states and health care utilization in older gay men.
Although HIV-related sexual risk behaviors have been studied extensively in adolescents and young adults, there is limited information about these behaviors among older Americans, which make up a growing segment of the US population and an understudied population. This review of the literature dealing with sexual behaviors that increase the risk of becoming HIV-infected found a low prevalence of condom use among older adults, even when not in a long-term relationship with a single partner. A seminal study by Schick et al published in 2010 reported that the prevalence of condom use at last intercourse was highest among those aged 50-59 years (24.3%; 95% confidence interval, 15.6-35.8) and declined with age, with a 17.1% prevalence among those aged 60-69 years (17.1%; 95% confidence interval, 7.3-34.2). Studies have shown that older Americans may underestimate their risk of becoming HIV-infected. Substance use also increases the risk for sexual risk behaviors, and studies have indicated that the prevalence of substance use among older adults has increased in the past decade. As is the case with younger adults, the prevalence of HIV infections is elevated among ethnic minorities, drug users (eg, injection drug users), and men who have sex with men. When infected, older adults are likely to be diagnosed with HIV-related medical disorders later in the course of illness compared with their younger counterparts. Physicians are less likely to discuss sexual risk behaviors with older adults and to test them for HIV compared with younger adults. Thus, it is important to educate clinicians about sexual risk behaviors in the older age group and to design preventive interventions specifically designed for older adults.


Gay and bisexual men (GBM) who participate in gay community subcultures have different profiles, including differing risk behaviors. We examined men's participation in gay community subcultures, and its association with risk behavior. In a cross-sectional survey, 849 GBM provided information about men in their personal networks. We devised measures of their participation in five subcultural groupings and explored their associations with sexual behavior. We identified five subcultural groupings: sexually adventurous; bear tribes; alternative queer; party scene; and sexually conservative. Higher scores on the sexually adventurous measure was associated with being older, having more gay friends, being HIV-positive, and being more sexually active. It was also independently associated with unprotected anal intercourse with casual partners (AOR 1.82; 95 % CI 1.20-2.76; p = 0.005). HIV prevention strategies need to account for the different subcultural groupings in which GBM participate. Measures of engagement with gay subcultures are useful indicators of differential rates of risk behavior and modes of participation in gay community life. Men in more sexually adventurous subcultures are more likely to engage in sexual risk behavior.


Background. Studying the most extreme example of late diagnosis, new HIV diagnoses after death, may be instructive to HIV testing efforts. Using the results of routine HIV testing of autopsies performed by the Office of Chief Medical Examiner (OCME), we identified new HIV diagnoses after death in New York City (NYC) from 2008 to 2012. Methods. Population-based registries for HIV and deaths were linked to identify decedents not known to be HIV-infected before death. Multivariable logistic regression models were constructed to determine correlates of a new HIV diagnosis after death among all persons newly diagnosed with HIV and among all HIV-infected decedents receiving an OCME autopsy. Results. Of 264 893 deaths, 24 426 (9.2%) were autopsied by the NYC OCME. Of these,
1623 (6.6%) were infected with HIV, including 142 (8.8%) with a new HIV diagnosis at autopsy. This represents 0.8% (142 of 18,542) of all new HIV diagnoses during the 5-year period. Decedents newly diagnosed with HIV at OCME autopsy were predominantly male (73.9%), aged 13-64 years (85.9%), non-white (85.2%), unmarried (81.7%), less than college educated (83.8%), and residents of an impoverished neighborhood (62.0%). Of all HIV-infected OCME decedents aged >/=65 years (n = 71), 22.0% were diagnosed at autopsy. The strongest independent correlate of new HIV diagnosis at autopsy in both multivariable models was age >/=65 years. Conclusions. Human immunodeficiency virus diagnoses first made after death are rare, but, when observed, these diagnoses are more commonly found among persons >/=65 years, suggesting that despite highly visible efforts to promote HIV testing community-wide, timely diagnosis among older adults living in impoverished, high-prevalence neighborhoods may require additional strategies.


BACKGROUND: Sustained or consistent use of condoms by men remains a challenge. A study was carried out to identify factors associated with failure to use condoms consistently by men attending STD clinics in Pune, India.

METHOD: Among 14137 STI clinic attendees, 8360 HIV sero-negative men were enrolled in a cohort study. The changes in condom usage behavior were studied among 1284 men who returned for first scheduled quarterly follow up, 309 reported consistent condom use at the time of enrollment in the cohort. Data pertaining to heterosexual men practicing high risk behavior were analyzed to identify factors associated with change in condom use behavior using logistic regression model. Demographic, behavioral and biological factors observed to be associated with condom use were fitted in five Cox proportional hazards models to calculate hazard ratios and their 95% confidence intervals to identify independent predictors of failure to sustain condom use behavior. RESULTS: The univariate analysis showed that men who were 30 years or older in age (p = 0.002) and those who did not have contact female sex worker (FSW) were more likely to fail to sustain consistent condom use. However both these factors did not show significant association in multivariable analysis. Marital status and contact with Hijra (eunuch) in lifetime were associated with failure to change in their condom use behavior [AOR 0.33 (CI 0.13-0.82; p = 0.017)]. During the follow up of 2 years, 61 events (15.5 per 100 person years, 95% CI 12.3-19.5 years) of 'failure of condom use' were recorded despite counseling. Older age, contact with non CSW partner and presence of genital ulcer disease / discharge syndrome were significant predictors of failure to sustain condom use. DISCUSSION: Married monogamous older men, who report contact with sex worker and present with genital ulcer disease are at risk of failure to use condom after first exposure to voluntary HIV counseling and testing. This is a scenario of primary prevention program. Condom promotion and counseling needs to be reinforced through follow up counseling among this population.


BACKGROUND: Human immunodeficiency virus (HIV) is a major public health concern in the United States, particularly among older Black women who comprise approximately 40% of the newly diagnosed cases among women. This systematic review sought to answer the research question: What are the sexual practices in older Black women associated with HIV risk? METHODS: CINAHL, PubMed, MEDLINE, and Web of Knowledge electronic databases were searched for English-language research studies published between 2003 and 2013 that focused on the HIV sexual risk practices of Black women over the age of 50. Using PRISMA guidelines, two reviewers independently reviewed and appraised the quality of relevant articles; agreement of select studies was achieved by consensus. RESULTS: Among the 3,167 articles surveyed, 9 met inclusion criteria. The majority (88%) were quantitative, observational studies. All nine articles addressed at least one of three factors that contribute to HIV sexual risk:
Behavioral (inconsistent condom use and multiple sexual partners), psychological (risk perception, depression/stress, trauma, and self-esteem issues), and social factors (economics, education, and drugs/alcohol use). Outcome measures varied across studies. CONCLUSION: Although this systematic review appraised few studies, findings suggest that many older Black women are engaged in HIV risk-taking practices. Clinicians and researchers need to be aware of the HIV risk practices of older Black women to improve health outcomes through education, effective communication and risk appraisal.


The African American church is a community-based organization that is integral to the lives, beliefs, and behaviors of the African American community. Engaging this vital institution as a primary setting for HIV testing and referral would significantly impact the epidemic. The disproportionately high HIV incidence rate among African Americans dictates the national priority for promotion of early and routine HIV testing, and suggests engaging community-based organizations in this endeavor. However, few multilevel HIV testing frameworks have been developed, tested, and evaluated within the African American church. This article proposes one such framework for promoting HIV testing and referral within African American churches. A qualitative study was employed to examine the perceptions, beliefs, knowledge, and behaviors related to understanding involvement in church-based HIV testing. A total of four focus groups with church leaders and four in-depth interviews with pastors, were conducted between November 2012 and June 2013 to identify the constructs most important to supporting Philadelphia churches' involvement in HIV testing, referral, and linkage to care. The data generated from this study were analyzed using a grounded theory approach and used to develop and refine a multilevel framework for identifying factors impacting church-based HIV testing and referral and to ultimately support capacity building among African American churches to promote HIV testing and linkage to care.


In South Africa, a large proportion of young women are in age disparate relationships which is believed to be a risk factor for human immunodeficiency virus (HIV). The aim of this study was to determine the generational effect of age disparity on HIV and sexually transmitted infections (STI) incidence. Socio-demographic and behavioural data were collected from women, aged 16 and older, who were followed for up to 24 months. Women who reported having a steady sexual partner older than themselves were categorised into: (1) non-age disparate partnerships (age difference between partners was 0-4 years); (2) intra-generational age disparate partnerships (5-9 year age gap between sexual partners) and (3) inter-generational age disparate partnerships (age gap of 10 years or more between sexual partners). Of the 1355 women included in the analysis, 759, 429 and 167 were in non-age disparate, intra-generational age disparate and inter-generational age disparate partnerships, respectively. Strong predictors of inter-generational age disparate partnerships include age, marital status and concurrency of sexual partners. No significant relationship between age disparity and risk of HIV acquisition was found. The highest crude STI incidence was observed among those in intra-generational age disparate relationships followed by those in non-age disparate relationships [31.86 (26.41-38.44) and 25.60 (21.92-29.91) per 100 person-years, respectively]. Reduction of multiple partnerships remains key to HIV prevention; however, in light of partner concurrency being more prevalent than individual concurrency partnerships, female-initiated HIV prevention options remain critical.


We assessed changes in self-reported sexual activity (SA) over 13 years among HIV-infected and uninfected women. The impact of aging and menopause on SA and unprotected anal or vaginal intercourse (UAVI) was examined among women in the Women's Interagency HIV Study (WIHS), stratifying by HIV status and detectable viral load among HIV-infected women. Generalized mixed linear models were fitted for each outcome, adjusted for relevant covariates. HIV-uninfected women evidenced higher levels of SA and UAVI than HIV-infected. The odds of SA declined by 62-64 % per decade of age. The odds of SA in a 6-month interval for women aged 40-57 declined by 18-22 % post-menopause (controlling for age). Among HIV+/detectable women only, the odds of any UAVI decreased by 17 % per decade of age; the odds of UAVI were unchanged pre-menopause, and then decreased by 28 % post-menopause. Elucidating the factors accounting for ongoing unprotected sex among older women should inform interventions.


BACKGROUND: There is limited evidence on the efficacy of post-exposure prophylaxis (PEP) for sexual exposures. We sought to determine the factors associated with adherence to treatment and describe the incidence of PEP failures in a Montreal clinic. METHODS: We prospectively assessed all patients consulting for PEP following sexual exposures from October 2000 to July 2014. Patients were followed at 4 and 16 weeks after starting PEP. Treatment adherence was determined by self-report at week 4. Multivariable logistic regression was used to estimate the factors predicting adherence to treatment. RESULTS: 3547 PEP consults were included. Patients were mainly male (92%), MSM (83%) and sought PEP for anal intercourse (72%). Seventy-eight percent (n = 2772) of patients received a prescription for PEP, consisting of Tenofovir/Emtracitabine (TVD) + Lopinavir/Ritonavir (LPV) in 74% of cases, followed by Zidovudine/Lamivudine (CBV) + LPV (10%) and TVD + Raltegravir (RAL) (8%). Seventy percent of patients were adherent to treatment. Compared to TVD+LPV, patients taking CBV+LPV were less likely to adhere to treatment (OR 0.58, 95% CI 0.44-0.75), while no difference was observed for patients taking TVD+RAL (OR 1.15, 95% CI 0.83-1.59). First-time PEP consults, older and male patients were also more adherent to treatment. Ten treated patients seroconverted (0.37%) during the study period, yet only 1 case can be attributed to PEP failure (failure rate = 0.04%). CONCLUSION: PEP regimen was associated with treatment adherence. Patients were more likely to be adherent to TVD-based regimens. Ten patients seroconverted after taking PEP; however, only 1 case was a PEP failure as the remaining patients continued to engage in high-risk behavior during follow-up. One month PEP is an effective preventive measure to avoid HIV infection.


Men who have sex with men (MSM) are the largest risk group in the US HIV epidemic and African American MSM (AA MSM) are disproportionately affected. Substance-abusing sexual minorities warrant attention as they are at elevated risk for HIV, yet are not a homogeneous risk group. The purpose of this study was to use latent class analysis to identify patterns of drug and alcohol use in a sample of 359 AA MSM and examine associations with sexual risk. Three classes were identified: Individuals who used multiple substances (poly-users) (18 %), alcohol/marijuana users (33 %) and individuals who had low probability of reporting drug or problematic alcohol use (50 %). Results from multivariate analysis indicate that poly-users were older and more likely to report sex exchange and recent sexually transmitted infection compared to the other classes. Alcohol and poly-users were more likely to report sex under the
influence. Identifying and defining substance use patterns can improve specification of risk groups and allocation of prevention resources.


OBJECTIVE: Late HIV testing (LT), defined as receiving an AIDS diagnosis within a year of one's first positive HIV test, is associated with higher HIV transmission, lower HAART effectiveness, and worse outcomes. Latinos represent 36% of LT in the US, yet research concerning LT among HIV cases in Puerto Rico is scarce. METHODS: Multivariable logistic regression analysis was used to identify factors associated with LT, and a Cochran-Armitage test was used to determine LT trends in an HIV-infected cohort followed at a clinic in Puerto Rico specialized in the management and treatment of HIV. RESULTS: From 2000 to 2011, 47% of eligible patients were late testers, with lower median CD4 counts (54 vs. 420 cells/mm3) and higher median HIV viral load counts (253,680 vs. 23,700 copies/mL) than non-LT patients. LT prevalence decreased significantly, from 47% in 2000 to 37% in 2011. In a mutually adjusted logistic regression model, males, older age at enrollment and past history of IDU significantly increased LT odds, whereas having a history of amphetamine use decreased LT odds. When the data were stratified by mode of transmission, it became apparent that only the category men who have sex with men (MSM) saw a significant reduction in the proportion of LT, falling from 67% in 2000 to 33% in 2011. CONCLUSION: These results suggest a gap in early HIV detection in Puerto Rico, a gap that decreased only among MSM. An evaluation of the manner in which current HIV-testing guidelines are implemented on the island is needed.


OBJECTIVES: The NIDA Clinical Trials Network trial of rapid HIV testing/counseling in 1281 patients was a unique opportunity to examine relationships among substance use, depressive symptoms, and sex risk behavior. METHODS: Past 6-month substance use; substance use severity (Drug Abuse Screening Test - 10); depressive symptoms (Quick Inventory of Depressive Symptomatology); and three types of sex risk behavior (unprotected sex occasions [USOs] with primary partners; USOs with nonprimary partners; and USOs while high/drunken) were assessed. Zero-inflated negative binomial analyses provided: probability and rate of sex risk behavior (in risk behavior subsample). RESULTS: Levels of sexual risk behavior were high, while variable across the three types of sex risk behaviors. Among the patients, 50.4% had engaged in USOs with primary partners, 42% in sex while drunk or high, and 23.8% in USOs with nonprimary partners. Similar factors were significantly associated with all three types of sex risk behaviors. For all types, problem drinking, cocaine use, and substance use severity had an exacerbating effect. Older age was associated with lower risk behavior; other relationship categories (eg, married, separated/divorced, cohabitating) were associated with greater risk behavior than was single status. Depressive symptoms were associated with decreased likelihood of USOs with a primary partner. CONCLUSIONS: Sexual risk behavior is common among individuals in outpatient substance abuse treatment. Results highlight problem drinking (eg, up to three-fold) and cocaine (eg, up to twice) in increasing sex risk behavior. They demonstrate the utility of distinguishing between partner types and presence/absence of alcohol/drugs during sex. Findings argue for the need to integrate sex risk reduction into drug treatment.

Uptake of the female condom (FC) in the United States has historically been low; inadequate promotion may be one barrier faced by potential users. We performed a content analysis of state and municipal health department Web sites to describe how the FC is being promoted for pregnancy and disease prevention. We found that only a slim majority (60.8%) of health department Web sites mention the FC at all and those that do include numerous inaccuracies in their messaging. These inaccuracies may discourage uptake of the FC or have a detrimental impact on the experience when using the product for the first time.


INTRODUCTION: Understanding the impact of curable sexually transmitted infections (STIs) on HIV transmissibility is essential for effective HIV prevention programs. Investigating the impact of longitudinally measured recurrent STIs on HIV seroconversion is the interest of the current paper. METHODS: In this prospective study, data from a total of 1456 HIV-negative women who enrolled in a HIV biomedical trial were used. It was hypothesized that women who had recurrent STI diagnoses during the study share a common biological heterogeneity which cannot be quantified. To incorporate this "unobserved" correlation in the analysis, times to HIV seroconversion were jointly modelled with repeated STI diagnoses using Cox regression with random effects. RESULTS AND DISCUSSION: A total of 110 HIV seroconversions were observed (incidence rate of 6.00 per 100 person-years). In a multivariable model, women who were diagnosed at least once were more likely to seroconvert compared to those who had no STI diagnosis [hazard ratio (HR): 1.63, 95% confidence interval (CI): 1.04, 2.57]; women who had recurrent STI diagnoses during the study were 2.5 times more likely to be at increased risk of HIV infection (95% CI: 1.35, 4.01) with an estimated frailty variance of 1.52, with p<0.001, indicating strong evidence that there is a significant correlation (heterogeneity) among women who had recurrent STIs. In addition to this, factors associated with incidence of STIs, namely not being married and having a new sexual partner during the study follow-up, were all significantly associated with increased risk for HIV seroconversion (HR: 2.92, 95% CI: 1.76, 5.01 and HR: 2.25, 95% CI: 1.63, 3.83 respectively). CONCLUSIONS: The results indicated that women who were at risk for STIs were also at risk of HIV infection. In fact, they share the similar risk factors. In addition to this, repeated STI diagnoses also increased women's susceptibility for HIV infection significantly. Decreasing STIs by increasing uptake of testing and treatment and reducing partner change plays a significant role in the trajectory of the epidemic.


Previous studies have reported that approximately 30% of men who have sex with men (MSM) in China have concurrent female partners. Men who have sex with men and women (MSMW) might "bridge" HIV transmission to their female sex partners. This study aimed to explore (a) motivations for why MSMW in China engage in relationships and sexual behaviors with female partners; (b) patterns of sexual behaviors and condom use between MSMW and their female partners; and (c) barriers to and strategies for encouraging MSMW and their female partners to undergo HIV testing. The authors conducted in-depth interviews with 30 MSMW in two urban cities in China, Guangzhou and Chengdu, and used thematic analysis methods to code and interpret the data. MSMW described family, social, and workplace pressures to have a female partner, and expressed futility about their ability to form stable same-sex relationships. Although participants reported concern about the risk of personally acquiring and transmitting HIV or other sexually transmitted infections (STIs) to their female partners, they described the challenges to using condoms with female partners. HIV-positive participants described how stigma restricted their ability to disclose their HIV status to female partners, and HIV-negative participants displayed less immediate concern about the need for female partners to undergo HIV testing. Participants described a range of possible strategies to
HIV testing among female partners. These findings highlight the urgent need for HIV risk reduction and testing interventions for Chinese MSMW in the context of heterosexual partnerships, and they also underscore the additional need for privacy and cultural sensitivity when designing future studies.

Psychosocial


It is now well documented that many of the key drivers of health reside in our everyday living conditions. In the last two decades, public health has urged political action on these critical social determinants of health (SDH). As noted by the World Health Organisation, encouraging action in this area is challenging. Recent research has argued that public health researchers need to gain a deeper understanding of the complex and changing rationalities of policymaking. This, it seems, is the crucial next step for social determinants of health research. In this paper, we turn our attention to the practitioners of 'the art of government', in order to gain insight into how to secure upstream change for the SDH. Through interviews with policy actors (including politicians, senior government advisors, senior public servants and experienced policy lobbyists) the research sought to understand the nature of government and policymaking, as it pertains to action on the SDH. Through exploring the policy process, we examine how SDH discourses, evidence and strategies align with existing policy processes in the Australian context. Participants indicated that approaches to securing change that are based on linear conceptualisations of the policy process (as often found in public health) may be seen as 'out of touch' with the messy reality of policymaking. Rather, a more dialogic approach that embraces philosophical and moral reasoning (alongside evidence) may be more effective. Based on our findings, we recommend that SDH advocates develop a deeper awareness of the political and policy structures and the discursive conventions they seek to influence within specific settings.


HIV stigma continues to affect the psychosocial wellbeing of people living with HIV (PLWH) and people living close to them (PLC). Literature unequivocally holds the view that HIV stigma and psychosocial wellbeing interact with and have an impact on each other. This study, which is part of a larger research project funded by the South Africa Netherlands research Programme on Alternatives in Development (SANPAD), responds to the lack of interventions mitigating the impactful interaction of HIV stigma and psychosocial wellbeing and tests one such intervention. The research objectives were to test the changeover-time in the psychosocial wellbeing of PLWH and PLC in an urban and a rural setting, following a comprehensive community-based HIV stigma reduction and wellness enhancement intervention. An experimental quantitative single system research design with a pre- and four repetitive post-tests was used, conducting purposive voluntary sampling for PLWH (n = 18) and snowball sampling for PLC (n = 60). The average age of participants was 34 years old. The five measuring instruments used for both groups were the mental health continuum short-form scale, the patient health questionnaire, the satisfaction with life scale, the coping self-efficacy scale and the spirituality wellbeing scale. No significant differences were found between the urban-rural
settings and data were pooled for analysis. The findings show that initial psychosocial wellbeing changes after the intervention were better sustained (over time) by the PLC than by the PLWH and seemed to be strengthened by interpersonal interaction. Recommendations included that the intervention should be re-utilised and that its tenets, content and activities be retained. A second intervention three to six months after the first should be included to achieve more sustainability and to add focused activities for the enhancement of psychosocial wellbeing. PLWH and PLC are to be encouraged to engage with innovative community mechanisms to make psychosocial wellbeing a way of life in the community at large.


It is widely known that older women are at lesser risk for sexual violence than younger women, but current inattention to older women in the gender-based violence (GBV) field has minimized the experiences of older women survivors at great detriment to their health and rights. For example, health providers seldom ask older women about their sexual activity and relationships, a neglect that leads to older women being excluded from necessary HIV testing and care as well as support services for abuse. This oversight is increasingly worrisome given the rise in new HIV infections among adults age 50 and older in recent years, with the majority of transmissions stemming from individuals unaware of their HIV-positive status. Building on sexual rights scholarship, this paper argues for an approach to public health interventions for GBV and HIV that acknowledges older women - their sexuality, sexual agency, and activity - so that health providers and advocates acknowledge and serve older survivors.


The goal of this mixed method study was to describe the psychosocial profile of HIV-infected persons identified as long-term nonprogressors (LTNP), and their experiences of nonprogression. Data were collected from 24 participants with a mean age of 48 years and a mean duration of infection of 14 years. Results show rather moderate levels of anxiety and depression symptoms and a modest mean score of social support. Participants adapted by using acceptance, positive restructuring, and active coping strategies. Seven themes marked the experience: (a) reacting to announcement and dealing with diagnosis, (b) valuing interpersonal relations and well-being, (c) making changes in life, (d) coping with stress, (e) dealing with health care, (f) beliefs about reasons for nonprogression, and (g) living positively while dreading progression. The findings enrich a field of knowledge that has had little attention so far and shed light on the psychosocial profile of LTNP and their experiences of nonprogression.


This study examined the relationship between resilience, social capital and self-rated health among 263 HIV-positive South Africans living in poverty, using questionnaires. Self-rated good health was predicted by younger age, trust in community-based organizations and having contacts of different religions. The findings highlight the importance of community-based networks and resources for care and support for persons living with HIV/AIDS in poor, rural areas. Furthermore, resilience, which also related positively to education and income, contributed positively to self-rated health, drawing attention to the interplay between resources at individual and community levels.

In the U.S., HIV is concentrated among men who have sex with men (MSM), some of whom have had female partners (MSMW). MSMW are disproportionately impacted by psychosocial vulnerabilities, like depression and substance use that increase sexually transmitted infection (STI) and HIV risk. Research on psychosocial vulnerability and HIV-related sexual risk among MSMW is warranted to reduce infection transmission among MSM and to prevent bridging to female partners. We analyzed data from Wave IV (2007-2008) of the National Longitudinal Study of Adolescent Health to assess psychosocial vulnerability and HIV risk-taking among MSMW. Using lifetime and past year sexual activity, we classified men as ever having sex with: women only (MSW), men only (MSMO) or MSMW, with further refined categorization of MSMW with male only partners in the past 12 months, only female partners in the past 12 months, and both male and female partners in the past 12 months (N = 6,945). We compared psychosocial vulnerability characteristics and HIV-related risk behaviors among the five categories of men. MSMW were more likely to report depression, suicidality, substance use, and incarceration than MSW and MSMO. Compared to MSW, MSMW with current female partners had greater odds of unprotected sex, exchange sex, and STI. MSMW with male partners in the past year had greater odds of multiple or concurrent partners in the past year. HIV risk and psychosocial vulnerability factors are elevated among MSMW, a priority population for HIV risk reduction. HIV risk reduction interventions should address this and heterogeneity of sexual partnerships among MSMW.


Despite efforts to eliminate it at the societal level, HIV stigma persists and continues to threaten the health of people living with HIV (PLWH). We tested whether social support, adaptive coping, and/or HIV identity centrality act as resilience resources by buffering people from the negative impact of enacted and/or anticipated stigma on stress and ultimately HIV symptoms. Ninety-three PLWH completed a survey, and data analyses tested for evidence of mediation and moderation. Results demonstrated that instrumental social support, perceived community support, and HIV identity centrality buffered participants from the association between anticipated stigma and HIV symptoms. That is, anticipated stigma was associated with HIV symptoms via stress only at low levels of these resources. No resources buffered participants from the impact of enacted stigma. Identifying and enhancing resilience resources among PLWH is critical for protecting PLWH from the harmful effects of stigma.


Social workers have played an integral role in society's response to the HIV/AIDS pandemic since the discovery of the disease. As the landscape of the epidemic has changed, so has the social work response to it. Social workers are, and have been, central to the success of TESTAZ (Test, Educate, Support, and Treat Arizona), which is a nontargeted, routine opt-out HIV screening program in the emergency department (ED) of Maricopa Medical Center. This article focuses on the crucial role social workers play in every stage of program development, implementation, and patient movement through the stages of the HIV care continuum. Social worker involvement with HIV-positive patients diagnosed in the ED is imperative to achieving patient viral suppression.

Social workers play an important role in recognizing and addressing barriers to retention in HIV care. Although there is a large body of literature and research supporting interventions that promote medication adherence, there is limited intervention research that addresses retention in care, the precursor to adherence. Despite many advances in HIV treatment, many African Americans are not engaged in regular care. In a systematic review, the literature was critically appraised to examine intervention research designed to retain HIV-infected African Americans in treatment. Only peer-reviewed studies published from January 2002 through October 2012 were examined. The initial search generated a total of 798 studies. However, of these, only 13 met the inclusion criteria. Results highlight interventions that can be replicated by social workers--such as the use of ancillary support services, the use of adherence manuals, and theory-based interventions--to engage this population in care. Policy implications are also discussed.


The population of older people living with HIV in the United States is growing. Little is known about specific challenges older HIV-infected women face in coping with the disease and its attendant stressors. To understand these issues for older women, we conducted semi-structured in-depth interviews with 15 women (13 African American, 2 Caucasian) 50 years of age and older (range 50-79 years) in HIV care in the southeastern United States, and coded transcripts for salient themes. Many women felt isolated and inhibited from seeking social connection due to reluctance to disclose their HIV status, which they viewed as more shameful at their older ages. Those receiving social support did so mainly through relationships with family and friends, rather than romantic relationships. Spirituality provided great support for all participants, although fear of disclosure led several to restrict connections with a church community. Community-level stigma-reduction programs may help older HIV-infected women receive support.


PURPOSE: Social support can positively influence patients' health outcomes through a number of mechanisms, such as increases in patients' adherence to medication. Although there have been studies on the influence of social support on medication adherence, these studies were conducted in Western settings, not in Asian settings where cultural and religious orientations may be different. The objective of this study was to assess the effects of cultural orientation and religiosity on social support and its relation to patients' medication adherence.

METHODS: This was a cross-sectional study of patients with chronic diseases in two tertiary hospitals in Selangor, Malaysia. Patients who agreed to participate in the study were asked to answer questions in the following areas: 1) perceived group and higher authority cultural orientations; 2) religiosity: organizational and non-organizational religious activities, and intrinsic religiosity; 3) perceived social support; and 4) self-reported medication adherence. Patients' medication adherence was modeled using multiple logistic regressions, and only variables with a P-value of <0.25 were included in the analysis. RESULTS: A total of 300 patients completed the questionnaire, with the exception of 40 participants who did not complete the cultural orientation question. The mean age of the patients was 57.6+/-13.5. Group cultural orientation, organizational religious activity, non-organizational religious activity, and intrinsic religiosity demonstrated significant associations with patients' perceived social support (r=0.181, P=0.003; r=0.230, P<0.001; r=0.135, P=0.019; and r=0.156, P=0.007, respectively). In the medication adherence model, only age, duration of treatment, organizational religious activity, and disease type (human immunodeficiency virus) were found
to significantly influence patients' adherence to medications (adjusted odds ratio [OR] 1.05, P=0.002; OR 0.99, P=0.025; OR 1.19, P=0.038; and OR 9.08, P<0.05, respectively). CONCLUSION: When examining religious practice and cultural orientation, social support was not found to have significant influence on patients' medication adherence. Only age, duration of treatment, organizational religious activity, and disease type (human immunodeficiency virus) had significant influence on patients' adherence.


We apply a social-ecological interpretive framework to understanding relationships among patient privacy, psychological health, social stigma, and continuity in care in the HIV treatment cascade in the rural southeastern US. This research was conducted as part of the 2013 comprehensive needs assessment for the Northeast Georgia Ryan White Consortium using an anthropologically informed mixed-methods design, and a deductive-inductive approach to thematic analysis of qualitative data obtained in interviews and focus groups with service providers and service utilizers. Our comprehensive needs assessment yielded two key components. First, we identified salient phenomena influencing introduction to, retention among, and satisfaction of patients in the Ryan White-coordinated treatment cascade in NE-GA. Second, we formulated actionable recommendations around leverage points identified in the current district-wide system of care. Results highlight spatial, institutional, and interpersonal aspects of the system of care that intersect around issues of patient privacy, psychological health, and social stigma. These intersections constitute pathways by which persons living with HIV are exposed to stigma and other negative social signals regarding their health status without sufficient access to behavioral health services. These negative issues, in turn, can erect significant barriers to long-term continuity in care.


Most studies of psychosocial predictors of disease progression in HIV have not considered norepinephrine (NE), a neurohormone related to emotion and stress, even though NE has been related to accelerated viral replication in vitro and impaired response to antiretroviral therapy (ART). We therefore examined NE, cortisol, depression, hopelessness, coping, and life event stress as predictors of HIV progression in a diverse sample. Participants (n = 177) completed psychological assessment, blood draws [CD4, viral load (VL)], and a 15 h urine sample (NE, cortisol) every 6 months over 4 years. Hierarchical linear modeling (HLM) was used to model slope in CD4 and VL controlling for ART at every time point, gender, age, race, SES, and initial disease status. NE (as well as depression, hopelessness, and avoidant coping) significantly predicted a greater rate of decrease in CD4 and increase in VL. Cortisol was not significantly related to CD4, but predicted VL increase. To our knowledge, this is the first study relating NE, in vivo, to accelerated disease progression over an extended time. It also extends our previous 2 year study by relating depressed mood and coping to accelerated disease progression over 4 years.


We conducted an anonymous survey of providers who care for older adults from 10 Veterans Affairs long-term-care facilities to assess their knowledge, beliefs, and confidence toward treating infections and antimicrobial
stewardship. The average score on 5 questions assessing knowledge was 3.6 out of 5.0 (95% confidence interval, 3.3-3.9), which supports a need for education regarding the care of older adults with infections.


INTRODUCTION: Women represent nearly one-quarter of the 71,300 people living with HIV in Canada. Within a context of widespread HIV-related stigma and discrimination and on-going risks to HIV disclosure, little is known about the influence of growing social, legal and public health surveillance of HIV on sexual activity and satisfaction of women living with HIV (WLWH). METHODS: We analyzed baseline cross-sectional survey data for WLWH (&ge;16 years, self-identifying as women) enrolled in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS), a multisite, longitudinal, community-based research study in British Columbia (BC), Ontario (ON) and Quebec (QC). Sexual inactivity was defined as no consensual sex (oral or penetrative) in the prior six months, excluding recently postpartum women (&lt;=6 months). Satisfaction was assessed using an item from the Sexual Satisfaction Scale for Women. Multivariable logistic regression analysis examined independent correlates of sexual inactivity. RESULTS: Of 1213 participants (26% BC, 50% ON, 24% QC), median age was 43 years (IQR: 35, 50). 23% identified as Aboriginal, 28% as African, Caribbean and Black, 41% as White and 8% as other ethnicities. Heterosexual orientation was reported by 87% of participants and LGBTQ by 13%. In total, 82% were currently taking antiretroviral therapy (ART), and 77% reported an undetectable viral load (VL&lt;40 copies/mL). Overall, 49% were sexually inactive and 64% reported being satisfied with their current sex lives, including 49% of sexually inactive and 79% of sexually active women (p&lt;0.001). Sexually inactive women had significantly higher odds of being older (AOR=1.06 per year increase; 95% CI=1.05-1.08), not being in a marital or committed relationship (AOR=4.34; 95% CI=3.13-5.88), having an annual household income below $20,000 CAD (AOR: 1.44; 95% CI=1.08-1.92), and reporting high (vs. low) HIV-related stigma (AOR=1.81; 95% CI=1.09-3.03). No independent association was found with ART use or undetectable VL. CONCLUSIONS: Approximately half of WLWH in this study reported being sexually inactive. Associations with sexual dissatisfaction and high HIV-related stigma suggest that WLWH face challenges navigating healthy and satisfying sexual lives, despite good HIV treatment outcomes. As half of sexually inactive women reported being satisfied with their sex lives, additional research is required to determine whether WLWH are deliberately choosing abstinence as a means of resisting surveillance and disclosure expectations associated with sexual activity. Findings underscore a need for interventions to de-stigmatize HIV, support safe disclosure and re-appropriate the sexual rights of WLWH.


HIV infection is concentrated in populations living in poverty. We examined the overlapping and independent effects of multiple poverty indicators on HIV-related health status. Because substance use can create competing survival needs when resources are limited, we also sought to objectively measure expenditures on food relative to alcohol and tobacco products. To achieve these aims, 459 men and 212 women living with HIV infection in Atlanta, GA completed measures of socio-demographic and heath characteristics as well as multiple indicators of poverty including housing stability, transportation, food insecurity, and substance use. Participants were given a $30 grocery gift card for their participation and we collected receipts which were coded for alcohol (beer, wine, liquors) and tobacco purchases. Results showed that participants with unsuppressed HIV replication were significantly more likely to experience multiple indicators of poverty. In addition, one in four participants purchased alcohol or tobacco products with their gift cards, with as much as one-fourth of money spent on these products. A multivariable logistic regression model showed that food insecurity was independently associated with unsuppressed HIV, and purchasing alcohol or tobacco products did not moderate this association. Results confirm previous research to show the primacy
of food insecurity in relation to HIV-related health outcomes. Competing survival needs, including addictive substances, should be addressed in programs that aim to alleviate poverty to enhance the health and well-being of people with HIV infection.


Previous research has identified an association between food insecurity and depression in a variety of world regions in both healthy and HIV-infected individuals. We examined this association in 183 HIV-infected Hispanic adults from the greater Boston area. We measured depression with the Burnam depression screen and food insecurity with the Radimer/Cornell Questionnaire. Dietary intake was assessed with an adapted version of the Block Food Frequency Questionnaire. Logistic regression models were created with depression as the outcome variable and food insecurity as the main predictor. In bivariate analyses, food insecurity was significantly associated with depression [odds ratio (OR) 2.5; 95% confidence interval (CI) 1.1, 5.5; p = 0.03]. When we accounted for social support, food insecurity was no longer significant. We found no differences in the quality or quantity of dietary intake between the food insecure and food secure groups. Our findings highlight the importance of social support in the association between food insecurity and depression. Food insecurity may reflect social support more than actual dietary intake in this population.


Little is known about the impact of HIV and aging on cognitive functioning. This New York City cross-sectional study of aging HIV-positive gay and bisexual men assessed their neuropsychological state. Working memory and verbal abstract reasoning were relatively intact. After 55 years of age, attention abilities were impaired. Executive function impairment was present regardless of age and education. Results suggest the need for HIV-specific norms, and the use of neuropsychological assessments (i.e. baseline and over time) as a cost-effective way to assess HIV-related cognitive decline in developed and under-developed countries.


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Recent statistics show a growing number of older adults who are living alone and are socially isolated. It is against this background that, in recent years, many interventions have been developed to address social isolation among the elderly. Evaluative studies show that most interventions are hardly effective, though. An important reason for this is the heterogeneity of the socially isolated. This article offers insight into this heterogeneity by presenting a typology with different profiles of socially isolated older adults and the intervention implications of this typology. The typology is derived from an extensive qualitative study on socially isolated elderly individuals in the Netherlands. The typology imposes some degree of order to a diversity of circumstances, ambitions, and possibilities of the socially isolated elderly, thereby deepening the understanding of the heterogeneity of this population. The definition of social isolation used in this study starts from a societal angle of incidence, namely the current policy context of Western European welfare states, in which governments emphasize the importance of independence and self-reliance of their citizens. Developed from that perspective, the typology provides a theoretical basis for applying interventions aimed at increasing self-reliance of social isolated elderly. This perspective on social isolation also has consequences for the way in which the effectiveness of interventions to alleviate social isolation is assessed.


Estimates suggest 30% of adults report the highest levels of loneliness. Though men are more likely than women to use illicit substances and engage in heavy drinking, the prevalence of substance use in women is growing and their escalation toward dependence occurs more rapidly. Loneliness and substance use have greater relevance within the HIV+ population, with higher rates of substance misuse than the general population. However, the association between loneliness and substance use within HIV+ individuals remains understudied. The purpose of the present study was to test the hypothesis that there would be an association between loneliness and substance moderated by gender in HIV+ older adults. A cross-sectional study was conducted between October 2013 and January 2014. Study participants included 96 HIV-positive Black/African American men and women recruited through the University of Florida Center for HIV/AIDS Research, Education and Service (UF CARES) in Jacksonville, Florida. Participants completed an interviewer-administered assessment examining mental and behavioral health. Pearson correlations examined associations between loneliness and substance use. Binary logistic regression analyses stratified by gender examined the association between loneliness and substance use while controlling for covariates. Among women, loneliness was associated with illicit drug use, AOR = 3.37, 95% CI: 1.23-9.21, p = .018 and heavy drinking, AOR = 2.47, 95% CI: 1.07-5.71, p = .033. No significant associations were found between loneliness and illicit drug use, and heavy drinking in men. Substance use among women in this population may be linked to loneliness. Interventions should be gender specific. Further research into this association is necessary as it will likely have important clinical implications for this population.

The Veterans Aging Cohort Study (VACS) Index was developed as a risk index for health outcomes in HIV, and it has been consistently associated with mortality. It shows a significant, yet relatively weak, association with neurocognitive impairment, and little is known about its utility among ethnic/racial minority groups. We examined whether the association between the VACS Index and neurocognition differed by ethnic/racial group. Participants included 674 HIV-infected individuals (369 non-Hispanic whites, 111 non-Hispanic blacks, and 194 Hispanics). Neurocognitive function was assessed via a comprehensive battery. Scaled scores for each neurocognitive test were averaged to calculate domain and global neurocognitive scores. Models adjusting for demographics and HIV disease characteristics not included in the VACS Index showed that higher VACS Index scores (indicating poorer health) were significantly associated with worse global neurocognition among non-Hispanic whites. This association was comparable in non-Hispanic blacks, but nonsignificant among Hispanics (with similar results for English and Spanish speaking). We obtained comparable findings in analyses adjusting for other covariates (psychiatric and medical comorbidities and lifestyle factors). Analyses of individual neurocognitive domains showed similar results in learning and delayed recall. For other domains, there was an effect of the VACS Index and no significant interactions with race/ethnicity. Different components of the VACS Index were associated with global neurocognition by race/ethnicity. In conclusion, the association between the VACS Index and neurocognitive function differs by ethnic/racial group. Identifying key indicators of HIV-associated neurocognitive impairment by ethnic/racial group might play an important role in furthering our understanding of the biomarkers of neuroAIDS.


More people are living with HIV into midlife and older age. Although increased longevity brings new hope, it also raises unanticipated challenges—especially for gay men who never thought they would live into middle and older age. Middle-aged and older people are more likely to face multiple comorbidities, yet many lack the necessary supports to help them adapt to the challenges of aging with HIV. This article presents the findings of a qualitative study developed to explore gay men's experience of aging with HIV. Multiple in-depth exploratory interviews were conducted with 15 gay-identified men living with HIV/AIDS over an 18-month period. A systematic strategy data analysis consistent with grounded theory revealed a pattern of subtle adjustments to living with HIV that resulted in diminishing circles of social support and social involvement. This dynamic is referred to as "a shrinking kind of life," an in-vivo code built from the participant's own words. Four themes from the research (physical challenges, a magnitude of loss, internal changes, & stigma) are discussed. Conclusions include recommendations for future research and implications for practice in the field. Practitioners knowledgeable of the factors that impact their social involvement can empower gay men through individual and group interventions to confront a shrinking kind of life and define for themselves what it means to optimally age with HIV.


As black women over age 50 represent a growing share of women living with HIV, understanding what helps them persist and engage in ongoing HIV care will become increasingly important. Delineating the specific roles of social support and stigma on HIV care experiences among this population remains unclear. We qualitatively examined how experiences with stigma and social support either facilitated or inhibited engagement in HIV care, from the perspective of older black women. Semi-structured interviews were conducted with 20 older black women currently receiving HIV care at primary care clinics in the Metropolitan Boston area. Women expressed that experiences with stigma and seeking support played an important role in evaluating the risks and benefits of engaging in care. Social support facilitated their ability to engage in care, while stigma interfered with their ability to engage in care.
throughout the course of their illness. Providers in particular, can facilitate engagement by understanding the changes in these women's lives as they struggle with stigma and disclosure while engaging in HIV care. The patient's experiences with social support and stigma and their perceptions about engagement are important considerations for medical teams to tailor efforts to engage older black women in regular HIV care.


Apathy remains a common neuropsychiatric disturbance in the Human Immunodeficiency Virus (HIV-1) despite advances in anti-retroviral treatment (ART). The goal of the current review is to recapitulate findings relating apathy to the deleterious biobehavioral effects of HIV-1 in the post-ART era. Available literatures demonstrate that the emergence of apathy with other neurocognitive and neuropsychiatric symptoms may be attributed to neurotoxic effects of viral proliferation, e.g., aggregative effect of Tat and gp120 on apoptosis, transport and other enzymatic reactions amongst dopaminergic neurons and neuroglia. An assortment of neuroimaging modalities converge on the severity of apathy symptoms associated with the propensity of the virus to replicate within frontal-striatal brain circuits that facilitate emotional processing. Burgeoning research into functional brain connectivity also supports the effects of microvascular and neuro-inflammatory injury linked to aging with HIV-1 on the presentation of neuropsychiatric symptoms. Summarizing these findings, we review domains of HIV-associated neurocognitive and neuropsychiatric impairment linked to apathy in HIV. Taken together, these lines of research suggest that loss of affective, cognitive and behavioral inertia is commensurate with the neuropathology of HIV-1.


We sought to understand the support networks of people living with HIV (PLWH) in the Canadian cities of Winnipeg and Regina, particularly of their network of caregivers and with a focus on people from disadvantaged and/or stigmatized communities. Using a variation of the Photovoice method, 31 study participants took photographs of their everyday realities and were then interviewed. Among the findings was the heavy reliance on institutional caregivers and on nonhuman sources of support. There was evidence of peer-to-peer networks of care, but the strongest connections were with their formal caregivers. HIV as a chronic condition among disadvantaged and/or stigmatized groups requires paying special attention to informal and formal care dynamics and to where social or family networks cannot meet the basic needs. Honing in on and enhancing these features through programs and services can only improve the situation of stigmatized yet hopeful and resilient PLWH.


High rates of cognitive impairment persist in human immunodeficiency virus (HIV) infection, despite improved health outcomes and reduced mortality through widespread use of antiretroviral therapy (ART). Heavy alcohol use and cigarette smoking are potential contributors to neurocognitive impairment in people living with HIV (PLWH), yet few studies have examined their influence concurrently. Here we investigated the effects of self-reported alcohol use and smoking on learning, memory, processing speed, verbal fluency, and executive function in 124 HIV-positive men who have sex with men [age (mean +/- SD) = 42.8 +/- 10.4 years], engaged with medical care. All participants were heavy drinkers. Duration of HIV infection averaged 9.9 +/- 7.6 years, and 92.7% were on a stable ART regimen. Participants completed a neuropsychological battery and assessment of past 30-day substance use. Average number
of drinks per drinking day (DPDD) was 5.6 +/- 3.5, and 33.1% of participants were daily smokers. Rates of neurocognitive impairment were the highest in learning (50.8%), executive function (41.9%), and memory (38.0%).

Multiple regression models tested DPDD and smoking status as predictors of neurocognitive performance, controlling for age and premorbid intelligence. Smoking was significantly, negatively related to verbal learning (p = .046) and processing speed (p = .001). DPDD was a significant predictor of learning (p = .047) in a model that accounted for the interaction of DPDD and smoking status. As expected, premorbid intelligence significantly predicted all neurocognitive scores (ps < .01), and older age was associated with slower processing speed (ps < .01). In conclusion, smoking appears to be associated with neurocognitive functioning deficits in PLWH beyond the effects of heavy drinking, aging, and premorbid intelligence. Smoking cessation interventions have the potential to be an important target for improving functional outcomes in heavy drinking PLWH.


This qualitative study aimed to identify the health-care problems of people living with HIV (PLHIV) in 2 large cities: Tehran and Kermanshah. Two main groups of stakeholders - service providers (policy-makers, managers, physicians and counsellors) and service recipients (PLHIV and their relatives) - participated in focus group discussions and in-depth interviews. We identified 24 themes covering the major health problems of PLHIV, including: incomplete and inadequate coverage of health-care services; patients' substance abuse; patients' fear of stigma; occupational burnout of certain service providers; patients' dissatisfaction with some of the services provided by counselling centres/clinics; medical staff's failure to observe confidentiality; and patients' lack of access to required specialized services. The problems and needs identified can inform the design and implementation of health programmes in our country and elsewhere in the Eastern Mediterranean Region.


The objective of this study was to examine gender roles in the provision and receipt of care among older Ugandans. Survey data on care work were collected in 2009-2010 from 510 older people infected or affected by HIV/AIDS, at one rural and one semi-urban site. The questionnaire was adapted from the WHO Study on global AGing and adult health survey. The type of care work done by older men and women for children in their households differs, yet, both men and women are taking on various types of care work. Women were more likely to report taking part in health/personal and physical care, whereas men were more likely to report providing financial assistance. Some older people, particularly women, were providing care at the same time as needing care. The finding on reciprocity of care suggests the need for further studies focused on how the reciprocity of care may affect health and well-being in older age.


HIV has increasingly impacted older adults regarding sero-prevalence and sero-incidence as long-term survivors of HIV/AIDS are living longer. This study examines the relationship between age and HIV-related attitudes and risk behaviors among female public housing residents in Puerto Rico. Using a self-administered survey instrument, 1,138 female public housing residents were surveyed between April and August 2006. Bivariate results showed that older women (aged 50+ years) were significantly less likely to report HIV testing and to discuss safer sex
with their most recent "steady" sex partner than women under the age of 50 years. Older women were also more likely to express anxiety associated with condoms and more barriers to using condoms. The older versus younger groups did not significantly differ regarding condom use, which was extremely low across the groups. In the past three and 12 months, older women were less likely than younger women to report having (a) multiple sex partners and; (b) oral and anal sex with their most recent steady sex partner; (c) oral sex with their most recent non-steady sex partner and, (d) engaging in sexual activity in the previous three and 12 months. Age-specific messages concerning their increased risk of HIV among other interventions would likely curtail the increase in the number of new HIV cases being reported among members of this sub-population.


In the last four decades, we have witnessed vast and important transitions in the social, economic, political, and health contexts of the lived experiences of gay men in the United States. This dynamic period, as evidenced most prominently by the transition of the gay rights movement to a civil rights movement, has shifted the exploration of gay men's health from one focusing primarily on HIV/AIDS into a mainstream consideration of the overall health and wellbeing of gay men. Against this backdrop, aging gay men in the United States constitute a growing population, for whom further investigations of health states and health-related disparities are warranted. In order to advance our understanding of the health and wellbeing of aging gay men, we outline here a multilevel, ecosocial conceptual framework that integrates salient environmental, social, psychosocial, and sociodemographic factors into sets of macro-, meso-, and micro-level constructs that can be applied to comprehensively study health states and health care utilization in older gay men.


PURPOSE OF THE STUDY: The National Institutes of Health calls for research that explores what it means to age optimally with HIV/AIDS as half of the U.S. people with HIV are aged 50 or older. This study applied the stress process model to examine the association between HIV stigma and psychological well-being and mediating resources (i.e., spirituality and complementory and integrative health [CIH] approaches) in older adults with HIV. DESIGN AND METHODS: Using data from the Research on Older Adults with HIV (ROAH) study, structural equation modeling was used to estimate these relationships within a latent variable model. Namely, a direct negative association between HIV stigma and psychological well-being was hypothesized that would be mediated by spirituality and/or CIH use. RESULTS: The analyses showed that the model fits the data well \( \chi^2 (137, N = 914) = 561.44, p = .000; \) comparative fit index = .964; root mean square error of approximation = .058, 95% confidence interval = .053 to .063]. All observed variables significantly loaded on their latent factor, and all paths were significant. Results indicated that spirituality and CIH use significantly mediated the negative association between HIV stigma and psychological well-being. IMPLICATIONS: Findings highlight the importance of spiritual and CIH interventions for older adults with HIV/AIDS. Practice recommendations are provided at the micro- and mesolevel.


BACKGROUND: Although the role of clinical/biological factors associated with mortality has already been explored in HIV-infected patients on antiretroviral therapy (ART), to date little attention has been given to the
potential role of social vulnerability. This study aimed to construct an appropriate measure of social vulnerability and to evaluate whether this measure is predictive of increased mortality risk in ART-treated patients followed up in the ANRS CO8 APROCO-COPILOTE cohort. METHODS: The cohort enrolled 1,281 patients initiating a protease inhibitor-based regimen in 1997-1999. Clinical/laboratory data were collected every 4 months. Self-administered questionnaires collected psycho-social/behavioural characteristics at enrolment (month \( M \) 0), M4 and every 8-12 months thereafter. A multiple correspondence analysis using education, employment and housing indicators helped construct a composite indicator measuring social vulnerability. The outcome studied was all-cause deaths occurring after M4. The relationship between social vulnerability and mortality, after adjustment for other predictors, was studied using a shared-frailty Cox model, taking into account informative study dropout. RESULTS: Over a median (IQR) follow-up of 7.9 (3.0-11.2) years, 121 deaths occurred among 1,057 eligible patients, corresponding to a mortality rate (95% CI) of 1.64 (1.37, 1.96)/100 person-years. Leading causes of death were non-AIDS defining cancers (n=26), AIDS (n=23) and cardiovascular diseases (n=12). Social vulnerability (HR [95% CI] =1.2 [1.0, 1.5]) was associated with increased mortality risk, after adjustment for other known behavioural and bio-medical predictors. CONCLUSIONS: Social vulnerability remains a major mortality predictor in ART-treated patients. A real need exists for innovative interventions targeting individuals cumulating several sources of social vulnerability, to ensure that social inequalities do not continue to lead to higher mortality.


OBJECTIVE: This study aimed to determine the combined effects of age and HIV infection on the risk of incident neurocognitive disorders. METHOD: A total of 146 neurocognitively normal participants were enrolled at baseline into one of four groups based on age (</= 40 years and >/= 50 years) and HIV serostatus resulting in 24 younger HIV-, 27 younger HIV+, 39 older HIV-, and 56 older HIV+ individuals. All participants were administered a standardized clinical neuropsychological battery at baseline and 14.3 +/- .2 months later. RESULTS: A logistic regression predicting incident neurocognitive disorders from HIV, age group, and their interaction was significant (chi(2)[4] = 13.56, p = .009), with a significant main effect of HIV serostatus (chi(2)[1] = 5.01, p = .025), but no main effect of age or age by HIV interaction (ps > .10). Specifically, 15.7% of the HIV+ individuals had an incident neurocognitive disorder as compared to 3.2% of the HIV- group (odds ratio = 4.8 [1.2, 32.6]). Among older HIV+ adults, lower baseline cognitive reserve, prospective memory, and verbal fluency each predicted incident neurocognitive disorders at follow-up. CONCLUSIONS: Independent of age, HIV infection confers a nearly fivefold risk for developing a neurocognitive disorder over approximately one year. Individuals with lower cognitive reserve and mild weaknesses in higher-order neurocognitive functions may be targeted for closer clinical monitoring and preventative measures.


BACKGROUND: To effectively meet the health care needs of multimorbid patients, the most important psychosocial factors associated with multimorbidity must be discerned. Our aim was to examine the association between self-reported adverse childhood experiences (ACEs) and multimorbidity and the contribution of other social, behavioural and psychological factors to this relationship. METHODS: We analysed cross-sectional data from the Mitchelstown study, a population-based cohort recruited from a large primary care centre. ACE was measured by self-report using the Centre for Disease Control ACE questionnaire. Multimorbidity status was categorized as 0, 1 or >/=2 chronic diseases, which were ascertained by self-report of doctor diagnosis. Ordinal logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) for multimorbidity, using ACE as the independent variable with adjustment for social (education, public health cover), behavioural (smoking, exercise, diet, body mass
RESULTS: Of 2047 participants, 45.3% (n = 927, 95% CI: 43.1-47.4) reported multimorbidity. ACE was reported by 28.4% (n = 248, 95% CI: 25.3-31.3%) of multimorbid participants, 21% (n = 113, 95% CI: 18.0-25.1%) of single chronic disease participants and 16% (n = 83, 95% CI: 13.2-19.7%) of those without chronic disease. The OR for multimorbidity with any history of ACE was 1.6 (95% CI: 1.4-2.0, P < 0.001). Adjusting for social, behavioural and psychological factors only marginally ameliorated this association, OR 1.4 (95% CI: 1.1-1.7, P = 0.002). CONCLUSIONS: Multimorbidity is independently associated with a history of ACEs. These findings demonstrate the psychosocial complexity associated with multimorbidity and should be used to inform health care provision in this patient cohort.


Older HIV-infected gay men may experience multiple forms of stigma related to sexual orientation (homonegativity), HIV (HIV stigma), and age (ageism), all of which can negatively impact quality of life (QOL). Our purpose was to determine predictors of homonegativity, internalized HIV stigma, and ageism, and stigma experiences that were predictive of QOL. Sixty HIV-infected gay men, ages 50-65 years, participated. Younger age and emotion-focused coping were significantly predictive of homonegativity, accounting for 28% of variance. Younger age, support group participation, medications per day, social support, and emotion-focused coping predicted internalized HIV stigma, accounting for 35% of variance. Problem-focused coping predicted ageism, accounting for 7% of variance. In regression analysis, the three types of stigma accounted for 39% of variance in QOL (homonegativity 19%, internalized HIV stigma 19%, ageism 0.5%). Study findings may help researchers develop interventions to alleviate multiple stigma experiences of HIV-infected older gay men, thus improving QOL.


The prevalence of HIV (human immunodeficiency virus) associated neurocognitive disorders (HAND) will undoubtedly increase with the improved longevity of HIV-infected persons. HIV infection, itself, as well as multiple physiologic and psychosocial factors can contribute to cognitive impairment and neurologic complications. These comorbidities confound the diagnosis, assessment, and interventions for neurocognitive disorders. In this review, we discuss the role of several key comorbid factors that may contribute significantly to the development and progression of HIV-related neurocognitive impairment, as well as the current status of diagnostic strategies aimed at identifying HIV-infected individuals with impaired cognition and future research priorities and challenges.


Antiretroviral (ARV) medication diversion to the illicit market has been documented in South Florida, and linked to sub-optimal adherence in people living with HIV. ARV diversion reflects an unmet need for care in vulnerable populations that have difficulty engaging in consistent HIV care due to competing needs and comorbidities. This study applies the Gelberg-Andersen behavioral model of health care utilization for vulnerable populations to understand how social vulnerability is linked to ARV diversion and adherence. Cross-sectional data were collected from a targeted sample of vulnerable people living with HIV in South Florida between 2010 and 2012 (n = 503). Structured interviews collected quantitative data on ARV diversion, access and utilization of care, and ARV adherence. Logistic regression was used to estimate the goodness-of-fit of additive models that test domain fit. Linear
regression was used to estimate the effects of social vulnerability and ARV diversion on ARV adherence. The best fitting model to predict ARV diversion identifies having a low monthly income and unstable HIV care as salient enabling factors that promote ARV diversion. Importantly, health care need factors did not protect against ARV diversion, evidence that immediate competing needs are prioritized even in the face of poor health for this sample. We also find that ARV diversion provides a link between social vulnerability and sub-optimal ARV adherence, with ARV diversion and domains from the Behavioral Model explaining 25% of the variation in ARV adherence. Our analyses reveal great need to improve engagement in HIV care for vulnerable populations by strengthening enabling factors (e.g., patient-provider relationship) to improve retention in HIV care and ARV adherence for vulnerable populations.


OBJECTIVE: Social control in the health domain refers to attempts by social network members to get an individual to modify their health behaviors. According to the dual effects model of social control, having one's health behavior controlled by others should be related to healthier behavioral change, but might arouse psychological distress as one may resent being controlled. Despite potential healthy behavior change, the stress of social control may thus be detrimental as interpersonal stress has been related to negative health outcomes. In the present study, the association between perceived social control and telomere length was tested to examine its association to biological outcomes. METHOD: In this cross-sectional study, a relatively healthy community sample of 140 middle age and older adults completed measures of perceived social control, perceived stress, and health behaviors. Peripheral blood mononuclear cells were used to determine telomere length. RESULTS: Main results showed that higher levels of perceived direct social network control were associated with shorter telomere length. These links were not influenced by statistical controls for medication use, self-rated health, trait hostility, and optimism. Perceived social control was also related to greater perceived stress but not health behaviors overall. However, neither perceived stress nor health behaviors mediated the link between social control and telomere length. CONCLUSIONS: Although the study design precludes strong inferences, these results suggest that perceived social control may be associated with cellular aging. These data also highlight the utility of integrating biological outcomes into social control models. (PsycINFO Database Record


This study is the first to examine the experiences and needs of an international sample of current, English-speaking, lesbian, transgender-identified (trans-lesbian) adults around a number of later life and end-of-life perceptions, preparations, and concerns. I analyzed a subset (n = 276) of the cross-sectional data collected from the online Trans MetLife Survey on Later-Life Preparedness and Perceptions in Transgender-Identified Individuals (N = 1,963). I assessed perceptions and fears around aging, preparation for later life, and end-of-life as well as numerous
demographic and psycho-social variables. Despite the overall feeling that they have aged successfully, the respondent trans-lesbian population harbors significant fears about later life. I found that this population, while better-prepared than the overall respondent trans-identified population, is still ill-prepared for the major legalities and events that occur in the later to end-of-life time periods.


The 1.5 million older adults who self-identify as lesbian, gay, bisexual, and transgender (LGBT) are expected to double in number by 2030. Research suggests that health disparities are closely linked with societal stigma, discrimination, and denial of civil and human rights. More LGBT older adults struggle with depression, substance abuse, social isolation, and acceptance compared to their heterosexual counterparts. Despite individual preferences, most health care providers recognize the right of any individual to have access to basic medical services. The U.S. Department of Health and Human Services requires that all hospitals receiving funds from Medicare and Medicaid respect visitation and medical decision-making rights to all individuals identifying as LGBT. The Joint Commission also requires a non-discrimination statement for accreditation. The current literature review examines LGBT health disparities and the consequential psychosocial impact on LGBT older adults as well as brings awareness to the needs of this underserved and underrepresented population.


INTRODUCTION: This paper aims to assess the extent and correlates of intimate partner violence (IPV), explore relationship power inequity and the role of sexual and social risk factors in the production of violence among young women aged 16-24 reporting more than one partner in the past three months in a peri-urban setting in the Western Cape, South Africa. Recent estimates suggest that every six hours a woman is killed by an intimate partner in South Africa, making IPV a leading public health problem in the country. While there is mounting evidence that levels of IPV are high in peri-urban settings in South Africa, not much is known about how it manifests among women who engage in concomitantly high HIV risk behaviours such as multiple sexual partnering, transactional sex and age mixing. We know even less about how such women negotiate power and control if exposed to violence in such sexual networks. METHODS: Two hundred and fifty nine women with multiple sexual partners, residing in a predominantly Black peri-urban community in the Western Cape, South Africa, were recruited into a bio-behavioural survey using Respondent Driven Sampling (RDS). After the survey, focus group discussions and individual interviews were conducted among young women and men to understand the underlying factors informing their risk behaviours and experiences of violence. FINDINGS: 86% of the young women experienced IPV in the past 12 months. Sexual IPV was significantly correlated with sex with a man who was 5 years or older than the index female partner (OR 1.7, 95% CI 1.0-3.2) and transactional sex with most recent casual partner (OR 2.1, 95% CI 1.1-3.8). Predictably, women experienced high levels of relationship power inequity. However, they also identified areas in their controlling relationships where they shared decision making power. DISCUSSION: Levels of IPV among young women with multiple sexual partners were much higher than what is reported among women in the general population and shown to be associated with sexual risk taking. Interventions targeting IPV need to address sexual risk taking as it heightens vulnerability to violence.
Treatment


BACKGROUND: Co-infection with human immunodeficiency virus (HIV) and Hepatitis-C virus (HCV) poses a significant threat to personal and public health. Substance use among co-infected persons leads to increased morbidity and mortality. The purpose of this study is to examine the continued substance use of people living with HIV-HCV co-infection and receiving antiretroviral therapy (ART).

METHODS: Individuals living with HIV infection in Atlanta, GA and currently receiving ART (N = 678) completed audio-computer-assisted self-interviews for demographic, health, and behavior characteristics; unannounced pill counts to assess ART adherence over one month; finger-stick blood specimens collected for HCV antibody testing and urine specimens for drug use screening; and obtained HIV viral load and CD4 cell counts from their medical provider. We performed cross-sectional analyses for behavioral and biological markers of health, health behaviors, and substance use.

RESULTS: Among participants, 131 (19%) were HIV-HCV co-infected; 53% were HIV-mono-infected, and 60% of HIV-HCV co-infected participants tested positive for use of at least one non-alcohol drug: tetrahydrocannabinol (THC) and cocaine were most prevalent. HIV-HCV co-infected individuals were older, with no other significant differences. Within the HIV-HCV co-infected participants, drug users (N = 87) did not differ from non-drug users (N = 53) in terms of ART adherence. However, drug users were significantly more likely to have uncontrolled HIV (17%) compared with those who did not test drug positive (4%).

CONCLUSIONS: Substance use is prevalent in persons with HIV-HCV co-infection and may interfere with ART. Research with a larger and more representative sample is needed to replicate and confirm these results.


Aging is now a well-recognized characteristic of the HIV-infected population and both AIDS and aging are characterized by a deficiency of the T-cell compartment. The objective of the present study was to evaluate the impact of antiretroviral (ARV) therapy in recovering functional response of T cells to both HIV-1-specific ENV peptides (ENV) and tetanus toxoid (TT), in young and aged AIDS patients who responded to ARV therapy by controlling virus replication and elevating CD4(+) T cell counts. Here, we observed that proliferative response of T-cells to either HIV-1-specific Env peptides or tetanus toxoid (TT) was significantly lower in older antiretroviral (ARV)-treated patients. With regard to cytokine profile, lower levels of IFN-gamma, IL-17 and IL-21, associated with elevated IL-10 release, were produced by Env- or TT-stimulated T-cells from older patients. The IL-10 neutralization by anti-IL-10 mAb did not elevate IFN-gamma and IL-21 release in older patients. Finally, even after a booster dose of TT, reduced anti-TT IgG titers were quantified in older AIDS patients and it was related to both lower IL-21 and IFN-gamma production and reduced frequency of central memory T-cells. Our results reveal that ARV therapy, despite the adequate recovery of CD4(+) T cell counts and suppression of viremia, was less efficient in recovering adequate immune response in older AIDS patients.


Optima is a software package for modeling HIV epidemics and interventions that we developed to address practical policy and program problems encountered by funders, governments, health planners, and program implementers. Optima’s key feature is its ability to perform resource optimization to meet strategic HIV objectives, including HIV-related financial commitment projections and health economic assessments. Specifically, Optima allows
users to choose a set of objectives (such as minimizing new infections, minimizing HIV-related deaths, and/or minimizing long-term financial commitments) and then determine the optimal resource allocation (and thus program coverage levels) for meeting those objectives. These optimizations are based on the following: calibrations to epidemiological data; assumptions about the costs of program implementation and the corresponding coverage levels; and the effects of these programs on clinical, behavioral, and other epidemiological outcomes. Optima is flexible for which population groups (specified by behavioral, epidemiological, and/or geographical factors) and which HIV programs are modeled, the amount of input data used, and the types of outputs generated. Here, we introduce this model and compare it with existing HIV models that have been used previously to inform decisions about HIV program funding and coverage targets. Optima has already been used in more than 20 countries, and there is increasing demand from stakeholders to have a tool that can perform evidence-based HIV epidemic analyses, revise and prioritize national strategies based on available resources, set program coverage targets, amend subnational program implementation plans, and inform the investment strategies of governments and their funding partners.


Background. Vitamin D insufficiency is prevalent in human immunodeficiency virus-positive (HIV+) persons. Human immunodeficiency virus and antiretroviral therapy (ART) may create unique risk factors, and the optimal vitamin D repletion and maintenance regimen in HIV+ persons remains unclear. Methods. Human immunodeficiency virus-positive adults on suppressive ART underwent routine serum 25-hydroxyvitamin D (25OHD) screening. Persons with vitamin D insufficiency (25OHD <30 ng/mL) received open-label, oral vitamin D3 50 000 international units (IU) twice weekly for 5 weeks, then 2000 IU daily to complete 12 weeks. We predicted 70% (95% confidence interval, 60%-80%) repletion to 25OHD >/=30 ng/mL compared with 85% among historical HIV-negative controls. Eighty participants provided 91% power to detect this difference. Ability to maintain 25OHD >/=30 ng/mL after 24 weeks was also assessed. Results. Baseline characteristics were similar between the 82 vitamin D insufficient and 40 sufficient persons enrolled: 95% male, 60% white, 88% nonsmokers, median age 49 years, body mass index 26 kg/m(2), and CD4(+) T lymphocyte count 520 cells/mm(3). After 12 weeks, 81% (66 of 82) of insufficient persons achieved 25OHD >/=30 ng/mL (P = .32 vs historical controls), with only older age (odds ratio [OR] = 1.06; P = .06), higher baseline 25OHD (OR = 1.14; P < .01), white race (OR = 3.39; P = .04), and current smoking (OR = 0.25; P = .06) associated with successful repletion. After 24 weeks, 73% (48 of 66) maintained 25OHD >/=30 ng/mL, with tenofovir (OR = 5.00; P = .01) and abacavir use (OR = 0.23; P = .02) associated with success and failure, respectively, to maintain 25OHD levels. Conclusions. The 25OHD repletion rates were comparable between HIV+ adults on suppressive ART and historical HIV-negative controls, indicating that successful oral repletion can be achieved in this population.


HIV infection is associated with chronic immune activation that is superimposed on immunologic senescence in older adults, resulting in the acquisition of age-related diseases at younger ages. The incidence of coronary artery disease is higher among HIV-infected persons than uninfected individuals matched for age and sex. HIV infection and its treatment have been associated with premature bone loss. Lung, hepatic, and anal cancers occur at younger ages in persons with HIV infection. HIV-infected patients are living longer, and proper attention to the management of comorbidities in this population is essential. This article summarizes an IAS-USA continuing education webinar presented by Howard Libman, MD, in January 2015.
INTRODUCTION: Statin therapy is effective in the prevention of cardiovascular disease in the general population but has been shown to modestly increase the risk for incident diabetes mellitus (DM). METHODS: We analyzed incident DM in HIV Outpatient Study (HOPS) participants followed at 8 HIV clinic sites during 2002-2011, comparing rates among those who initiated statin therapy during that period with those who did not. Using Cox proportional hazards models, we examined the association between cumulative years of statin exposure and the risk of developing DM, after controlling for age, sex, race/ethnicity, antiretroviral history, prevalent hepatitis C, body mass index, and cumulative exposure to protease inhibitor therapy. We also adjusted for propensity scores to account for residual confounding by indication. RESULTS: Of 4692 patients analyzed, 590 (12.6%) initiated statin therapy and 355 (7.2%) developed DM. Incident DM was independently associated with statin therapy (adjusted hazard ratio, 1.14 per year of statin use), as well as older age, Hispanic/Latino ethnicity, non-Hispanic/Latino black race, antiretroviral-naive status, prevalent hepatitis C, and body mass index >/=30 kg/m(2) (P < 0.05 for all). The association of statin use with incident DM was similar in the model adjusted for propensity score. CONCLUSIONS: Statin use was associated with a modestly increased risk of incident DM in an HIV-infected population, similar to existing data for the general population. HIV-infected patients should be monitored for glucose intolerance, but statins should not be withheld if clinically indicated for cardiovascular disease risk reduction.

OBJECTIVES: This study aimed to describe the epidemiology and risk factors of cholelithiasis and nephrolithiasis among HIV-positive patients in the era of combination antiretroviral therapy. METHODS: We retrospectively reviewed the medical records of HIV-positive patients who underwent routine abdominal sonography for chronic viral hepatitis, fatty liver, or elevated aminotransferases between January 2004 and January 2015. Therapeutic drug monitoring of plasma concentrations of atazanavir was performed and genetic polymorphisms, including UDP-glucuronosyltransferase (UGT) 1A1*28 and multidrug resistance gene 1 (MDR1) G2677T/A, were determined in a subgroup of patients who received ritonavir-boosted or unboosted atazanavir-containing combination antiretroviral therapy. Information on demographics, clinical characteristics, and laboratory testing were collected and analyzed. RESULTS: During the 11-year study period, 910 patients who underwent routine abdominal sonography were included for analysis. The patients were mostly male (96.9%) with a mean age of 42.2 years and mean body-mass index of 22.9 kg/m2 and 85.8% being on antiretroviral therapy. The anchor antiretroviral agents included non-nucleoside reverse-transcriptase inhibitors (49.3%), unboosted atazanavir (34.4%), ritonavir-boosted lopinavir (20.4%), and ritonavir-boosted atazanavir (5.5%). The overall prevalence of cholelithiasis and nephrolithiasis was 12.5% and 8.2%, respectively. Among 680 antiretroviral-experienced patients with both baseline and follow-up sonography, the crude incidence of cholelithiasis and nephrolithiasis was 4.3% and 3.7%, respectively. In multivariate analysis, the independent factors associated with incident cholelithiasis were exposure to ritonavir-boosted atazanavir for >2 years (adjusted odds ratio [AOR], 6.29; 95% confidence interval [CI], 1.12-35.16) and older age (AOR, 1.04; 95% CI, 1.00-1.09). The positive association between duration of exposure to ritonavir-boosted atazanavir and incident cholelithiasis was also found (AOR, per 1-year exposure, 1.49; 95% CI, 1.05-2.10). The associated factors with incident nephrolithiasis were hyperlipidemia (AOR, 3.97; 95% CI, 1.32-11.93), hepatitis B or C coinfection (AOR, 3.41; 95% CI, 1.09-10.62), and exposure to abacavir (AOR, 12.01; 95% CI, 1.54-93.54). Of 180 patients who underwent therapeutic drug monitoring of plasma atazanavir concentrations and pharmacogenetic investigations, we found that the atazanavir concentrations and UGT 1A1*28 and MDR1 G2677T/A polymorphisms were not statistically significantly associated with incident cholelithiasis and nephrolithiasis. CONCLUSIONS: In HIV-positive patients in the...
era of combination antiretroviral therapy, a high prevalence of cholelithiasis and nephrolithiasis was observed, and exposure to ritonavir-boosted atazanavir for >2 years was associated with incident cholelithiasis.


BACKGROUND: Anaemia has been linked with mortality in HIV infection. The mechanism of anaemia in the era of contemporary antiretroviral therapy is not understood. The aim of this study was to describe the association between anaemia and markers of immune activation and inflammation in a cohort of HIV-infected adults on stable antiretroviral therapy. METHODS: We performed a cross-sectional study of HIV-infected adults on antiretroviral therapy with HIV-1 RNA<1,000 copies/ml. Soluble and cellular markers of inflammation and immune activation were measured. Relationships between haemoglobin levels, anaemia (haemoglobin <13 g/dl for men and <12 g/dl for women) and mild anaemia (haemoglobin <14 g/dl for men and <13 g/dl for women) and these markers were explored using multivariable linear regression. RESULTS: Among the 147 participants, median age was 46 years, 78% were men, 68% were African American and 29% were Caucasian. Median body mass index (BMI) was 26.7 kg/m(2), nadir and current CD4(+) T-cell counts were 179 and 613 cells/mm(3), respectively, and 78% had HIV-1 RNA<50 copies/ml (range 20-600 copies/ml). Median (IQR) haemoglobin was 14.3 (13.1-15.1) g/dl; 14% were anaemic and 33% had at least mild anaemia. In multivariable analyses, mild anaemia was independently associated with female sex, older age, shorter duration of antiretroviral therapy, lower white blood cell count, higher platelet count, higher sCD14 and a greater number of CD14(dim)CD16(+) cells or 'patrolling' monocytes, which remained significant after further adjusting for race and BMI. CONCLUSIONS: Having haemoglobin <14 g/dl for men and <13 g/dl for women was independently associated with monocyte activation (sCD14 and CD14(dim)CD16(+) cells) in HIV-infected adults on stable antiretroviral therapy.


BACKGROUND: Recommendations have differed nationally and internationally with respect to the best time to start antiretroviral therapy (ART). We compared effectiveness of three strategies for initiation of ART in high-income countries for HIV-positive individuals who do not have AIDS: immediate initiation, initiation at a CD4 count less than 500 cells per μL, and initiation at a CD4 count less than 350 cells per μL. METHODS: We used data from the HIV-CAUSAL Collaboration of cohort studies in Europe and the USA. We included 55,826 individuals aged 18 years or older who were diagnosed with HIV-1 infection between January, 2000, and September, 2013, had not started ART, did not have AIDS, and had CD4 count and HIV-RNA viral load measurements within 6 months of HIV diagnosis. We estimated relative risks of death and of death or AIDS-defining illness, mean survival time, the proportion of individuals in need of ART, and the proportion of individuals with HIV-RNA viral load less than 50 copies per mL, as would have been recorded under each ART initiation strategy after 7 years of HIV diagnosis. We used the parametric g-formula to adjust for baseline and time-varying confounders. FINDINGS: Median CD4 count at diagnosis of HIV infection was 376 cells per μL (IQR 222-551). Compared with immediate initiation, the estimated relative risk of death was 1.02 (95% CI 1.01-1.02) when ART was started at a CD4 count less than 500 cells per μL, and 1.06 (1.04-1.08) with initiation at a CD4 count less than 350 cells per μL. Corresponding estimates for death or AIDS-defining illness were 1.06 (1.06-1.07) and 1.20 (1.17-1.23), respectively. Compared with immediate initiation, the mean survival time at 7 years with a strategy of initiation at a CD4 count less than 500 cells per μL was 2 days shorter (95% CI 1-2) and at a CD4 count less than 350 cells per μL was 5 days shorter (4-6). 7 years after diagnosis of HIV, 100%, 98.7% (95% CI 98.6-98.7), and 92.6% (92.2-92.9) of individuals would have been in need of ART with immediate initiation, initiation at a CD4 count less than 500 cells per μL, and initiation at a CD4 count less than 350 cells per
muL, respectively. Corresponding proportions of individuals with HIV-RNA viral load less than 50 copies per mL at 7 years were 87.3% (87.3-88.6), 87.4% (87.4-88.6), and 83.8% (83.6-84.9). INTERPRETATION: The benefits of immediate initiation of ART, such as prolonged survival and AIDS-free survival and increased virological suppression, were small in this high-income setting with relatively low CD4 count at HIV diagnosis. The estimated beneficial effect on AIDS is less than in recently reported randomised trials. Increasing rates of HIV testing might be as important as a policy of early initiation of ART. FUNDING: National Institutes of Health.


BACKGROUND: Tesamorelin, a synthetic analog of human growth hormone-releasing factor, decreases visceral adipose tissue (VAT) in human immunodeficiency virus (HIV)-infected patients with lipodystrophy. OBJECTIVES: 1) To evaluate the utility of patient characteristics and validated disease-risk scores, namely indicator variables for the metabolic syndrome defined by the International Diabetes Federation (MetS-IDF) or the National Cholesterol Education Program (MetS-NCEP) and the Framingham Risk Score (FRS), as predictors of VAT reduction during tesamorelin therapy at 3 and 6 months, and 2) To explore the characteristics of patients who reached a threshold of VAT <140 cm², a level associated with lower risk of adverse health outcomes, after 6 months of treatment with tesamorelin. METHODS: Data were analyzed from two Phase 3 studies in which HIV-infected patients with excess abdominal fat were randomized in a 2:1 ratio to receive tesamorelin 2 mg (n = 543) or placebo (n = 263) subcutaneously daily for 6 months, using ANOVA and ANCOVA models. RESULTS: Metabolic syndrome (MetS-IDF or MetS-NCEP) and FRS were significantly associated with VAT at baseline. Presence of metabolic syndrome ([MetS-NCEP], triglyceride levels >1.7 mmol/L, and white race had a significant impact on likelihood of response to tesamorelin after 6 months of therapy (interaction p-values 0.054, 0.063, and 0.025, respectively). No predictive factors were identified at 3 months. The odds of a VAT reduction to <140 cm² for subjects treated with tesamorelin was 3.9 times greater than that of subjects randomized to placebo after controlling for study, gender, baseline body mass index (BMI) and baseline VAT (95% confidence interval [CI] 2.03; 7.44). CONCLUSIONS: Individuals with baseline MetS-NCEP, elevated triglyceride levels, or white race were most likely to experience reductions in VAT after 6 months of tesamorelin treatment. The odds of response of VAT <140 cm² was 3.9 times greater for tesamorelin-treated patients than that of patients receiving placebo.


Adequate engagement in HIV care is necessary for the achievement of optimal health outcomes and for the reduction of HIV transmission. Positive Charge (PC) was a national HIV linkage and re-engagement in care program implemented by AIDS United. This study describes three PC programs, the characteristics of their participants, and the continuum of engagement in care for their participants. Eighty-eight percent of participants were engaged in care post PC enrollment. Sixty-nine percent were retained in care, and 46% were virally suppressed at follow-up. Older participants were more likely to be engaged, retained, and virally suppressed. Differences by race and gender in HIV care and treatment varied across PC programs, reflecting the diverse target populations, locations, and strategies employed by the PC grantees. There is an urgent need for programs that promote HIV care and treatment among vulnerable populations, including young people living with HIV. There is also an urgent need for additional research to test the effectiveness of promising linkage and retention in care strategies, such as peer navigation.

BACKGROUND: Strong international commitment and the widespread use of antiretroviral therapy have led to higher longevity for people living with human immune deficiency virus (HIV). Text messaging interventions have been shown to improve health outcomes in people living with HIV. The objectives of this overview were to: map the state of the evidence of text messaging interventions, identify knowledge gaps, and develop a framework for the transfer of evidence to other chronic diseases. METHODS: We conducted a systematic review of systematic reviews on text messaging interventions to improve health or health related outcomes. We conducted a comprehensive search of PubMed, EMBASE (Exerpta Medica Database), CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, Web of Science (WoS) and the Cochrane Library on the 17th April 2014. Screening, data extraction and assessment of methodological quality were done in duplicate. Our findings were used to develop a conceptual framework for transfer. RESULTS: Our search identified 135 potential systematic reviews of which nine were included, reporting on 37 source studies, conducted in 19 different countries. Seven of nine (77.7%) of these reviews were high quality. There was some evidence for text messaging as a tool to improve adherence to antiretroviral therapy. Text messages also improved attendance at appointments and behaviour change outcomes. The findings were inconclusive for self-management of illness, treatment of tuberculosis and communicating results of medical investigations. The geographical distribution of text messaging research was limited to specific regions of the world. Prominent knowledge gaps included the absence of data on long term outcomes, patient satisfaction, and economic evaluations. The included reviews also identified methodological limitations in many of the primary studies. CONCLUSIONS: Global evidence supports the use of text messaging as a tool to improve adherence to medication and attendance at scheduled appointments. Given the similarities between HIV and other chronic diseases (long-term medications, life-long care, strong link to behaviour and the need for home-based support) evidence from HIV may be transferred to these diseases using our proposed framework by integration of HIV and chronic disease services or direct transfer.


We sought to review the effectiveness of interventions designed to improve adherence to antiretroviral therapy (ART) from studies included in a recent Cochrane review that reported a clinical and an adherence outcome, with at least 80% follow-up for 6 months or more. Data were extracted independently and in duplicate, with an adjudicator for disagreements. Risk of bias was assessed using the Cochrane Risk of Bias tool. Of 182 relevant studies in the Cochrane review, 49 were related to ART. Statistical pooling was not warranted due to heterogeneity in interventions, participants, treatments, adherence measures and outcomes. Many studies had high risk of bias in elements of design and outcome ascertainment. Only 10 studies improved both adherence and clinical outcomes. These used the following interventions: adherence counselling (two studies); a once-daily regimen (compared to twice daily); text messaging; web-based cognitive behavioral intervention; face-to-face multi-session intensive behavioral interventions (two studies); contingency management; modified directly observed therapy; and nurse-delivered home visits combined with telephone calls. Patient-related adherence interventions were the most frequently tested. Uniform adherence measures and higher quality studies of younger populations are encouraged.


Diabetes mellitus (DM) is a common condition with significant associated morbidity and mortality. DM diagnosis and management among human immunodeficiency virus (HIV)-infected patients is a particularly relevant
topic as the HIV-infected population ages and more HIV-infected individuals live with chronic medical comorbidities. Although there is mixed evidence regarding HIV as an independent risk factor for DM, multiple factors related to HIV and its treatment are associated with DM. This review covers the epidemiology of DM in HIV-infected patients, and diagnosis, management, and treatment goals for DM in HIV-infected patients. We highlight the most recent DM treatment guidelines from the American Diabetes Association and the European Association for the Study of Diabetes, emphasizing individualization of DM medication therapy and treatment goals. Finally, we review a comprehensive approach to cardiovascular disease risk reduction in HIV-infected patients with DM and measures to prevent other complications of DM.


This qualitative study aimed to identify the health-care problems of people living with HIV (PLHIV) in 2 large cities: Tehran and Kermanshah. Two main groups of stakeholders - service providers (policy-makers, managers, physicians and counsellors) and service recipients (PLHIV and their relatives) - participated in focus group discussions and in-depth interviews. We identified 24 themes covering the major health problems of PLHIV, including: incomplete and inadequate coverage of health-care services; patients' substance abuse; patients' fear of stigma; occupational burnout of certain service providers; patients' dissatisfaction with some of the services provided by counselling centres/clinics; medical staff's failure to observe confidentiality; and patients' lack of access to required specialized services. The problems and needs identified can inform the design and implementation of health programmes in our country and elsewhere in the Eastern Mediterranean Region.


BACKGROUND: Group support psychotherapy (GSP) is a culturally sensitive intervention that aims to treat depression by enhancing social support, teaching coping skills, and income-generating skills. We compared GSP with group HIV education (GHE) for treatment of depression in people with HIV in Uganda. METHODS: In this open-label randomised controlled trial, we included men and women with HIV, aged 19 years or older, who met the Mini International Neuropsychiatric Interview criteria for major depression from an urban HIV care centre in Kitgum district, northern Uganda. Participants were randomly assigned to receive eight weekly sessions of either GSP or GHE. Randomisation was achieved by urn (men and women separately picked a paper containing the intervention allocation from a basket; ratio 1:1), and the intervention sessions were given to gender-specific groups. Participants were followed up immediately after the intervention and 6 months after the end of treatment. The primary outcomes were change in depressive symptom scores (measured with the Self-Reporting Questionnaire) and in function scores (measured with a locally developed method), analysed by intention to treat using cluster-adjusted t tests and permutation tests. This trial is registered with The Pan African Clinical Trials Registry, number PACTR201402000742370. FINDINGS: Between Jan 6, and Jan 20, 2014, we assessed 150 individuals, of whom 109 were randomly assigned to receive eight weekly sessions of either GSP (n=57) or GHE (n=52). Change in mean depression scores immediately after intervention did not differ between groups (mean difference -0.19, 95% CI -1.77 to 1.39, p=0.78). Mean function scores did not differ between groups either (0.24, -0.41 to 0.88; p=0.41). At 6 months after end of treatment, participants in the GSP group had lower mean depression scores than did those in the GHE group (-2.50, -3.98 to 1.02, p value=0.005), and higher function scores (0.74, -0.17 to 1.65, p=0.09) than did participants in the GHE group. No adverse events were reported. INTERPRETATION: The benefits of existing HIV educational interventions in HIV care services could be improved by the addition of GSP content. Potential benefits of
the integration of GSP into existing HIV interventions, such as adherence counselling or group HIV educational programmes, should be addressed in future studies. FUNDING: Grand Challenges Canada.


Knowledge that older people are vulnerable to develop tuberculosis is rarely considered in developing country settings. According to 2010 Global Burden of Disease estimates, the majority of tuberculosis-related deaths occurred among people older than 50; most in those aged 65 and above. Older people also contribute a large proportion of Disability-Adjusted Life Years (DALYs); 51% of tuberculosis DALYs occurred in patients aged 50 years and older in East Asia. Tuberculosis age distributions in Africa have been severely skewed by the human immunodeficiency virus (HIV) epidemic, but emerging data suggest increasing disease burdens among older people. Older adults are more likely to develop extra-pulmonary and atypical forms of disease that are often harder to diagnose than conventional sputum smear-positive pulmonary tuberculosis. Their care is complicated by more frequent drug-related adverse events and increased co-morbidity, which may prove difficult to manage in regions where health resources are already constrained. Health systems will have to confront the challenge of an ageing global population and the integrated services required to address their health needs.


The public health response to HIV/AIDS has turned its focus onto optimizing health care system delivery to maximize case identification, access and sustained engagement in antiretroviral treatment (ART). Opioid Agonist Treatment (OAT) provides a critical opportunity for HIV testing and linkage to ART. The EHOST study is a cluster-randomized, stepped-wedge trial to evaluate a prescriber-focused intervention to increase HIV testing rates, and optimize ART engagement and retention outcomes among individuals engaged in OAT. The study will encompass all drug treatment clinics currently admitting patients for the treatment of opioid use disorder across the province of British Columbia, encompassing an estimated 90% of the OAT caseload. The trial will be executed over a 24-month period, with groups of clinics receiving the intervention in 6-month intervals. Evaluation of the proposed intervention’s effectiveness will focus on three primary outcomes: (i) the HIV testing rate among those not known to be HIV positive; (ii) the rate of ART initiation among those not on ART; and (iii) the rate of ART continuation among those on ART. A difference-in-differences analytical framework will be applied to estimate the intervention’s effect. This approach will assess site-specific changes in primary outcomes across clusters while adjusting for potential residual heterogeneity in patient case mix, volume, and quality of care across clinics. Statistical analysis of outcomes will be conducted entirely with linked population-level administrative health datasets. Facilitated by established collaborations between key stakeholders across the province, the EHOST intervention promises to optimize HIV testing and care within a marginalized and hard-to-reach population.


BACKGROUND: Continued debate exists about whether initiation of antiretroviral therapy (ART) in symptom-free patients at higher baseline CD4 cell counts results in important clinical benefits. We aimed to examine to what extent baseline CD4 cell count at linkage to HIV care and at ART initiation predicts mortality in adults with HIV in Rwanda. METHODS: We included data for patients with HIV in Rwanda who were aged 15 years or older and linked to care or initiated ART between Jan 1, 1997, and April 30, 2014, from nationally representative databases. We analysed
the effect on mortality of baseline CD4 cell count at ART initiation and at linkage to care. Follow-up time was measured from time of ART initiation and from linkage to HIV care to study exit. To account for effect modification by time, we stratified by era of linkage (before 2008 vs 2008 or after) and for other indications for initiation of ART. We also stratified CD4 cell count by indication to initiate ART other than CD4 cell count status. We used Cox proportional hazard regressions to examine the effect of CD4 cell count at linkage and at ART initiation on mortality. FINDINGS: Our analysis was based on data from 50,147 patients who initiated ART and 72,061 patients linked to care. In the late era (2008 and after), linkage to care at a CD4 cell count of 100-199 cells per μL without any further indication was associated with higher mortality than linkage at 200-349 cells per μL (hazard ratio [HR] 1.37, 95% CI 0.95-1.97); the effect was much the same for initiation of ART in this CD4 stratum (1.37, 0.92-2.04). For higher CD4 strata, linkage to care at 500 cells per μL or more was protective (0.53, 0.39-0.72), whereas the reported effect of initiation of ART on mortality was not distinguishable from chance alone (0.82, 0.21-3.20). INTERPRETATION: Efforts are needed to link and retain patients early in pre-ART HIV care. In settings where ART is not yet available for immediate treatment, retention in a strong pre-ART programme is effective at improving survival. FUNDING: The Bill & Melinda Gates Foundation.


OBJECTIVE: This study aimed to determine the utility of 24-hour ambulatory blood pressure monitoring (ABPM) in a priori normotensive and known hypertensive people living with HIV by quantifying new hypertension (HTN), masked hypertension, uncontrolled BP, and white coat effect. DESIGN AND METHOD: Data analysed was from the Register of cardiovascular Complications among people living with HIV (RECOVIH), including 263 HIV+ individuals with 1 or more CV risk factors who underwent 24-h ABPM in our cardiac centre. Diagnostic criteria: Elevated clinic BP: at or above 140/90 mmHg. Elevated mean 24-h ABPM: at or above 130/80 mmHg, systolic and/or diastolic. New hypertension: elevated clinic BP and/or elevated mean 24-h ABPM. Masked hypertension: normal clinic BP and elevated mean 24-h ABPM. Uncontrolled BP: elevated clinic BP and/or elevated mean 24 h ABPM, in known HTN. White coat effect: elevated clinic BP and normal mean 24-h ABPM, in a priori normotensives. RESULTS: The cohort had a mean age of 50.3 +/- 7.7 years, was predominantly male (91%), had a long median HIV duration (15.3 years), and included 150 (57%) known HTN. In RECOVIH the prevalence of new HTN was 22% (n = 25), of which 50% masked hypertension diagnosed by 24-h ABPM solely. Uncontrolled HTN prevalence was 45% using clinic BP alone and 32% using 24-h ABPM alone. 24-h ABPM revealed that this masked uncontrolled HTN was frequently due to poor nocturnal BP control. White coat effect prevalence was not significantly different between the 2 groups (6.3% a priori normotensives vs. 9.3% known HTN, p = 0.37). HTN subjects were older, had higher BMI, and more frequently had a history of diabetes, coronary heart disease, and heart failure as compared to normotensives. CONCLUSIONS: Masked hypertension prevalence is high in RECOVIH, particularly among a priori normotensives. Suboptimal BP control is frequent among patients with treated and well-controlled clinic BP. Clinic BP monitoring alone is inadequate to diagnose HTN and assess true BP control because elevated nocturnal BP was frequent. These findings suggest ABPM should be more routinely used to diagnose HTN and confirm BP control in people living with HIV.


In the last four decades, we have witnessed vast and important transitions in the social, economic, political, and health contexts of the lived experiences of gay men in the United States. This dynamic period, as evidenced most prominently by the transition of the gay rights movement to a civil rights movement, has shifted the exploration of gay men's health from one focusing primarily on HIV/AIDS into a mainstream consideration of the overall health and
wellbeing of gay men. Against this backdrop, aging gay men in the United States constitute a growing population, for whom further investigations of health states and health-related disparities are warranted. In order to advance our understanding of the health and wellbeing of aging gay men, we outline here a multilevel, ecosocial conceptual framework that integrates salient environmental, social, psychosocial, and sociodemographic factors into sets of macro-, meso-, and micro-level constructs that can be applied to comprehensively study health states and health care utilization in older gay men.


**BACKGROUND & AIMS:** To compare the management of chronic hepatitis B (CHB) and its evolution over time in currently followed HIV-positive and HIV-negative patients. **METHODS:** A total of 709 consecutive patients with past or present positive HBs antigenemia seen in October 2012 in 19 French participating centres were included. The data were retrospectively collected from the first visit onwards through standardized questionnaires. **RESULTS:** Chronic hepatitis B was less often assessed in the 299 HIV-positive patients, who were older, more likely to be male, excessive alcohol drinkers and HBe antigen-, HCV- and HDV-positive. They were also followed up for a longer time (11.3 +/- 8.8 vs. 8.6 +/- 6.9 years, P < 10(-3) ) and were more frequently treated for HBV (95.3% vs. 56.8%, P < 10(-3) ). HBV was undetectable at the last visit in 80.8% of HIV-positive vs. 55.1% of HIV-negative patients (P < 10(-3) ). In multivariate analyses, undetectable HBV was significantly associated with older age, lower baseline HBV DNA, longer HBV therapy and no previous lamivudine monotherapy, but not with HIV. Cirrhosis was associated with age, male gender, Asian origin, alcoholism, HCV, HDV, but not with HIV infection. Hepatocellular carcinoma, less frequently observed in HIV-positive patients (0.7% vs. 4.7%, P = 0.002), was positively associated with age, male gender, cirrhosis and negatively associated with HIV infection (OR 0.15, 95%CI 0.03-0.67, P = 0.01). **CONCLUSIONS:** Although the assessment of CHB still has to be improved in HIV-positive patients, the negative impact of HIV on the virological, histological and clinical evolution of CHB seems to be disappearing, probably because of the immunovirological impact of HAART and the more frequent and longer use of HBV therapy.


**BACKGROUND:** As HIV management has become more successful during the past years, non-communicable diseases have become more prevalent among HIV-infected individuals. As a result, more HIV-infected patients die of cardiovascular diseases, with diabetes being one of the main risk factors. This study evaluates screening and management of diabetes among HIV-infected patients in a university hospital in the Netherlands. **METHODS:** We examined clinical characteristics, glycaemic control and cardiovascular risk management of HIV-infected patients with coexisting diabetes, and determined the frequency of diabetes screening in those without. **RESULTS:** Of 518 HIV-infected patients, 28 had been diagnosed with diabetes (5.4%), mostly (20/28) after being diagnosed with HIV. Patients with coexisting diabetes were older, had a longer duration of HIV, lower CD4 cell counts and higher body mass index (BMI), and were more likely to use aspirin, statins and antihypertensive medication than those without diabetes (all p &lt; 0.05). HbA1c values were below 7% (53 mmol/mol) in 54% of patients. Targets for systolic blood pressure (&lt; 140 mmHg), LDL cholesterol (&lt; 2.5 mmol/l) and BMI (&lt; 25 kg/m2) were achieved by 82%, 50% and 29% of patients, respectively. Annual ophthalmology examination, screening for microalbuminuria and foot control were rarely performed. Among the patients without known diabetes, diabetes screening during the past year had been performed using (non-fasting) plasma glucose in 56% and HbA1c in 10%, but 42% of patients had not been screened. **CONCLUSION:** For HIV-infected individuals with diabetes, glycaemic control and cardiovascular risk
management were reasonable, but screening for microvascular complications was rarely performed. Annual diabetes screening of HIV-infected patients was not routine.


BACKGROUND: Real-time adherence monitoring is now possible through medication storage devices equipped with cellular technology. We assessed the effect of triggered cell phone reminders and counseling using objective adherence data on antiretroviral therapy (ART) adherence among Chinese HIV-infected patients. METHODS: We provided ART patients in Nanning, China, with a medication device (Wisepill) to monitor their ART adherence electronically. After 3 months, we randomized subjects within optimal (/>=95%) and suboptimal (<95%) adherence strata to intervention vs. control arms. In months 4-9, intervention subjects received individualized reminders triggered by late dose taking (no device opening by 30 minutes past dose time) and counseling using device-generated data. Controls received no reminders or data-informed counseling. We compared postintervention proportions achieving optimal adherence, mean adherence, and clinical outcomes. RESULTS: Of 120 subjects enrolled, 116 (96.7%) completed the trial. Preintervention optimal adherence was similar in intervention vs. control arms (63.5% vs. 58.9%, respectively; P = 0.60). In the last intervention month, 87.3% vs. 51.8% achieved optimal adherence [risk ratio (RR): 1.7, 95% confidence interval (CI): 1.3 to 2.2] and mean adherence was 96.2% vs. 89.1% (P = 0.003). Among preintervention suboptimal adherers, 78.3% vs. 33.3% (RR: 2.4, CI: 1.2 to 4.5) achieved optimal adherence and mean adherence was 93.3% vs. 84.7% (P = 0.039). Proportions were 92.5% and 62.9% among optimal adherers, respectively (RR: 1.5, CI: 1.1 to 1.9) and mean adherence was 97.8% vs. 91.7% (P = 0.028). Postintervention clinical outcomes were not significant. CONCLUSIONS: Real-time reminders significantly improved ART adherence in this population. This approach seems promising for managing HIV and other chronic diseases and warrants further investigation and adaptation in other settings.


BACKGROUND: As antiretroviral treatments prolong life in HIV-infected patients, smoking cessation is now a top priority. However, studies of HIV-infected smokers have not been conducted with uninfected controls. We determined factors associated with contemplating smoking cessation and making a prior quit attempt among HIV-infected and uninfected smoking Veterans. METHODS: Between 2005 and 2007, we identified 1027 HIV-infected and 794 uninfected smokers enrolled in the Veterans Aging Cohort Study (VACS). Stratifying by HIV status, we calculated adjusted odds ratios using logistic regression to identify factors associated with contemplating smoking cessation and making a prior quit attempt. RESULTS: Most participants (66% of HIV-infected vs. 68% of uninfected, p=0.46) were contemplating cessation, and 56% of both groups (p=0.99) had attempted to quit in the last year. In stratified multivariable analyses, HIV-infected smokers with recent pulmonary disease diagnoses were more likely to have made a quit attempt (AOR 4.93, 95% CI=1.41-17.17). Both HIV-infected and uninfected patients with unhealthy alcohol use were less likely to be contemplating cessation (AOR 0.66, 95% CI=0.49-0.90 and 0.71, 95% CI=0.50-1.00). HIV-infected smokers who reported unhealthy alcohol use were also less likely to have made a quit attempt in the last year (AOR 0.68, 95% CI=0.51-0.91). CONCLUSIONS: Patient-level interest and motivation are not major barriers to smoking cessation among HIV-infected Veterans. Targeting HIV-infected smokers with a recent pulmonary disease diagnosis may improve sustained smoking cessation. Unhealthy alcohol use appears to be a key modifiable risk factor. Smoking cessation rates may be improved by combining interventions for smoking and alcohol use for HIV-infected patients.

During incarceration, many HIV-infected prisoners receive care and are adherent to medication. However, following release, many have difficulty engaging in HIV care and remaining on antiretroviral therapy. Community-based service providers for HIV-infected releasees have a deep understanding of the health needs and challenges these individuals face on community re-entry. We conducted in-depth qualitative interviews with 38 health care and service professionals in two southern U.S. states regarding the barriers releasees faced in meeting their health needs, including HIV care and treatment post release. Individual, community, and organization-level barriers to HIV care and treatment adherence post release were identified, and offered unique insight into the ways that these multilevel obstacles affect HIV-infected former prisoners' abilities to engage in care and access necessary social services. Provider perspectives should be considered when designing interventions to support HIV care after release.


BACKGROUND: The population infected with HIV is getting older and these people will increasingly develop age-related non-communicable diseases (NCDs). We aimed to quantify the scale of the change and the implications for HIV care in the Netherlands in the future. METHODS: We constructed an individual-based model of the ageing HIV-infected population, which followed patients on HIV treatment as they age, develop NCDs—including cardiovascular disease (hypertension, hypercholesterolaemia, myocardial infarctions, and strokes), diabetes, chronic kidney disease, osteoporosis, and non-AIDS malignancies—and start co-medication for these diseases. The model was parameterised by use of data for 10 278 patients from the national Dutch ATHENA cohort between 1996 and 2010. We made projections up to 2030. FINDINGS: Our model suggests that the median age of HIV-infected patients on combination antiretroviral therapy (ART) will increase from 43.9 years in 2010 to 56.6 in 2030, with the proportion of HIV-infected patients aged 50 years or older increasing from 28% in 2010 to 73% in 2030. In 2030, we predict that 84% of HIV-infected patients will have at least one NCD, up from 29% in 2010, with 28% of HIV-infected patients in 2030 having three or more NCDs. 54% of HIV-infected patients will be prescribed co-medications in 2030, compared with 13% in 2010, with 20% taking three or more co-medications. Most of this change will be driven by increasing prevalence of cardiovascular disease and associated drugs. Because of contraindications and drug-drug interactions, in 2030, 40% of patients could have complications with the currently recommended first-line HIV regimens. INTERPRETATION: The profile of patients in the Netherlands infected with HIV is changing, with increasing numbers of older patients with multiple morbidities. These changes mean that, in the near future, HIV care will increasingly need to draw on a wide range of medical disciplines, in addition to evidence-based screening and monitoring protocols to ensure continued high-quality care. These findings are based on a large dataset of HIV-infected patients in the Netherlands, but we believe that the overall patterns will be repeated elsewhere in Europe and North America. The implications of such a trend for care of HIV-infected patients in high-burden countries in Africa could present a particular challenge. FUNDING: Medical Research Council, Bill & Melinda Gates Foundation, Rush Foundation, and Netherlands Ministry of Health, Welfare and Sport.


OBJECTIVES: To investigate the prevalence of endocrine disturbances in a group of HIV-positive (HIV+) women and to identify factors affecting presence of these disorders. To examine specifically whether cellular ageing, as measured by leukocyte telomere length (LTL), is correlated with the presence of endocrine disturbance. DESIGN: A cross-sectional retrospective substudy of an ongoing prospective cohort study. PATIENTS: Adult HIV+ (≥19 years)
women enrolled in the CARMA (Children and Women: AntiRetrovirals and Markers of Aging) cohort study (N = 192). Prevalences of T2DM, glucose intolerance, dyslipidaemia, thyroid disorders, adrenal insufficiency, hypogonadism, primary ovarian insufficiency (POI), demographics, HIV and hepatitis C virus (HCV) infection status, baseline LTL, combined antiRetroviral therapy (cART) and substance exposures were collected. Statistical analysis included univariable followed by multivariable Poisson regression and step-wise reduction to refine the multivariable model. RESULTS: Prevalence of any endocrine abnormality was 58% (dyslipidaemia 43%, glucose intolerance/T2DM 13%, thyroid disorders 15%). In multivariable analysis, age was associated with number and type (any, glucose, lipid) of abnormality, while increasing body mass index (BMI) was associated with number of diagnoses and with glucose metabolism disorders. Interestingly, peak HIV pVL >/=100 000 copies/ml was associated with any abnormality, total number of disorders and presence of a thyroid disorder, while any disorder, glucose abnormalities and dyslipidaemia were negatively associated with alcohol use. LTL was not associated with number or type of endocrine abnormalities in this study. CONCLUSION: Further studies examining the relationship between duration and extent of exposure to HIV viraemia in relation to developing abnormal endocrine function are warranted.


INTRODUCTION: Tobacco use has emerged as a leading killer among persons living with HIV, with effective approaches to tobacco treatment still unknown. HIV infection is nearly 3 times as prevalent in Latinos than in non-Latino Whites. This study reports the results of a randomized trial comparing a tailored intervention to brief counseling for smoking cessation among Latino smokers living with HIV (LSLWH). METHODS: LSLWH (N = 302; 36% female, 10% employed full-time, 49% born in United States) were randomized to 4 in-person sessions of a tailored intervention (Aurora) or 2 in-person sessions of brief advice (enhanced standard care [ESC]). Both groups received 8 weeks of nicotine replacement therapy (NRT) patch. Biochemically validated 6- and 12-month 7-day point-prevalence abstinence (PPA) rates were compared, along with secondary outcomes (e.g., reduction to light smoking, NRT adherence). RESULTS: Seven-day PPA rates reached 8% versus 11% at 6 months and 6% versus 7% at 12 months, for Aurora and ESC, respectively, with no between-group differences (p values > .40). Significant changes from baseline to 6 and 12 months among intervention targets were noted (percentage reduction in heavy smoking and dependence; increases in knowledge and self-efficacy). Baseline smoking frequency, older age, and higher intensity of patch use during the trial emerged as significant predictors of abstinence at 6 months. CONCLUSIONS: There was no evidence that the tailored intervention improved cessation rates. Interventions that encourage use of, and adherence to, empirically validated cessation aids require further development to reduce tobacco-related death and disease in this vulnerable population.


BACKGROUND: Despite the dramatically improved survival due to combination antiretroviral therapies (cART), life expectancy of people with HIV/AIDS remains lower than that of the general population. This study aimed to estimate, at a population level, the survival experience of Italian people with AIDS (PWA) and to quantify the prognostic role of selected factors at diagnosis in the risk of early mortality (i.e., within six months from AIDS diagnosis). METHODS: A population-based, retrospective-cohort study was conducted among Italian PWA diagnosed between 1999 and 2009 and recorded in the national AIDS registry. The vital status, up to December 2010, of 14,552 PWA was ascertained through a record linkage procedure with the Italian mortality database. Survival probabilities were estimated through Kaplan-Meier method. To identify risk factors for early mortality from any cause, odds ratios (ORs) and corresponding 95% confidence intervals (CIs), adjusted for major confounders, were computed using
multivariate logistic regression models. RESULTS: Of the 5,706 deaths registered among the 14,552 PWA included in the study, 2,757 (18.9%) occurred within six months from AIDS diagnosis. The probability of surviving six months increased from 81.2% in PWA diagnosed in 1999-2000 to 82.9% in 2009, while the 5-year survival augmented from 60.7% in PWA diagnosed in 1999-2000 to 65.4% for PWA diagnosed in 2005-2006. Elevated risks of early mortality were associated to older age (OR = 5.28; 95% CI: 4.41-6.32 for age >/=60 vs. <35 years), injecting drug use (OR = 1.71; 95% CI: 1.53-1.91 vs. heterosexual intercourse), and CD4 count <50 cells/mm(3) at AIDS diagnosis (OR = 1.87, 95% CI: 1.55-2.27 vs. >/=500). Elevated ORs for early mortality also emerged for PWA diagnosed with primary brain lymphoma (OR = 11.66, 95% CI: 7.32-18.57), or progressive multifocal leukoencephalopathy (OR = 4.21, 95% CI: 3.37-5.27). CONCLUSIONS: Our study documented, among Italian PWA, the high-though slightly decreasing-frequency of early mortality in the full cART era. These findings indicate the need for enduring and ameliorating preventive actions aimed at timely HIV testing among all individuals at risk for HIV infection and/or those who present diseases known to be related with HIV infection.


Patient navigation, a patient-centered model of care coordination focused on reducing barriers to care, is an emerging strategy for linking patients to and retaining them in HIV care. The Guide to Healing Program (G2H), implemented at the Infectious Diseases Clinic at UNC Chapel Hill, provided patient navigation to women of color (WOC) new to or re-engaging in HIV care through a 'nurse guide' with mental health training and experience. The purpose of this study was to qualitatively explore patients' experiences working with the nurse guide. Twenty-one semi-structured telephone interviews with G2H participants were conducted. Interviews were transcribed and thematic analysis was utilized to identify patterns and themes in the data. Women's experiences with the nurse guide were overwhelmingly positive. They described the nurse guide teaching them critical information and skills, facilitating access to resources, and conveying authentic kindness and concern. The findings suggest that a properly trained nurse in this role can provide critical medical and psychosocial support in order to eliminate barriers to engagement in HIV care, and successfully facilitate patient HIV self-management. The nurse guide model represents a promising approach to patient navigation for WOC living with HIV.


CONTEXT AND OBJECTIVE: Adherence to antiretroviral treatment (ART) is not a stable condition, but is dynamic, like mental conditions. The aim of this study was to examine whether non-adherence to ART is related to demographic and immunological variables, substance use and presence of depressive symptoms. DESIGN AND SETTING: This was a cross-sectional prevalence study carried out at a public AIDS treatment center in the city of Sao Paulo, Brazil, between July 2006 and January 2007. METHODS: 438 patients on regular ART schedules with recent laboratory tests answered a demographic questionnaire, questions about substance use, the Hamilton Depression Rating Scale (HDRS) and the Simplified Medication Adherence Questionnaire (SMAQ). RESULTS: The prevalence of non-adherence over the past three months (a pattern of treatment interruption) was 46.3%, and 27.2% also reported this in the past week (a pattern of missed doses). ART interruption was significantly related to older age, lower CD4+ cell count and homosexual/bisexual transmission. The pattern of missed doses was significantly related to younger age, higher HDRS scores and higher viral load of RNA HIV. CONCLUSION: ART interruption may reflect recall errors and changes to the Brazilian demographic characteristics of HIV infection. The missed doses may reflect lifestyle characteristics of younger individuals. Attendance for HIV-positive individuals, particularly younger patients, should involve interventions and counseling in relation to the presence of depressive symptoms.


The article presents a clinical update on HIV infection and ageing, focusing on the role of aged care workers and nurses in caring for older people with HIV. Topics discussed include treatment of HIV with antiretrovirals (ARVs), patient adherence to treatments and its side effects, and pharmacy dispensing of ARVs. Other topics include the risk of getting HIV infection, mental health issues of HIV in older people, and discriminatory behaviour towards people with HIV.


The relationship between markers of monocyte/macrophage activation (sCD14 and sCD163) and components of the Veterans Aging Cohort Study (VACS) score, which predict mortality in patients with HIV, in immunologic nonresponders (INRs) is not defined. HIV+ subjects with >12 months of continuous virologic suppression and persistent CD4 <250 cells/mm³ were enrolled at the CORE Center, Chicago. Subjects had a single visit where history was taken and blood drawn. ELISA assays for sCD14 and sC163 were performed at Blood Systems, CA. Descriptive statistics were performed using SAS. We enrolled 43 subjects with persistent CD4 <250 after a median of 32 months of continuous viral suppression. We found elevated markers of monocyte/macrophage activation; sCD14 and sCD163 correlated with higher VACS scores as well as hepatitis C virus (HCV) coinfection and FIB-4 score, components of the VACS index. In this cohort of immunologic nonresponders, there was a significant correlation between markers of monocyte/macrophage activation and the VACS score. Among components of the VACS index, we did not find a significant association between HCV coinfection and sCD14; however, there was a significant association between HCV coinfection and sCD163.


OBJECTIVES: Deficits in cognitive function remain prevalent in HIV-infected individuals. The aim of this European multicentre study was to assess factors associated with cognitive function in antiretroviral therapy (ART)-naive HIV-infected subjects at the time of enrolment in the NEAT 001/Agence Nationale de Recherche sur le SIDA (ANRS) 143 study. METHODS: Prior to starting ART, seven cognitive tests exploring domains including episodic memory, verbal fluency, executive function and psychomotor speed were administered with scores standardized to z-score using the study population sample mean and standard deviation. The primary measure was overall z-score average (NPZ). We assessed associations between baseline factors and test results using multivariable regression models. RESULTS: Of 283 subjects with baseline cognitive assessments, 90% were male and 12% of black ethnicity. Median (interquartile range) age, years of education, years of known HIV infection, baseline CD4 count and baseline HIV RNA were 39 (31, 47) years, 13 (11, 17) years, 1 (0, 4) years, 344 (279, 410) cells/μL and 4.74 (4.28, 5.14) log10 HIV-1 RNA copies/mL, respectively. Forty per cent were current smokers. Factors significantly associated with poorer overall cognitive performance in multivariable models included older age, shorter duration of education, black ethnicity, lower height, and lower plasma HIV RNA. CONCLUSIONS: In this large, European-wide, ART-naive population with relatively preserved immunity and early HIV infection, cognitive function scores at the time of ART initiation were associated with demographic and HIV-disease factors.

PURPOSE OF REVIEW: With the overwhelming success of combination antiretroviral therapy, HIV infection is now a chronic, but manageable, medical condition. Consequently, HIV-infected cohorts are ageing leading to new challenges in the life-long management of this condition. Here, we review recent data concerning the modern treatment of older HIV-infected adults. RECENT FINDINGS: HIV-infected cohorts are ageing with the majority of those infected predicted to be more than 50 years old within the next 2 decades. There is emerging evidence of increased antiretroviral drug exposure in older individuals, but the evidence this leads to increased toxicity is less clear-cut. In addition, the choice of antiretroviral agents is more challenging in older HIV-infected patients because of the presence of comorbidities, which occur more commonly and at a younger age than in HIV-uninfected individuals and because of a higher propensity for drug-drug interactions due to the use of concomitant medications. Specific recommendations regarding antiretroviral treatment of older HIV-infected individuals are lacking and prospective trials in older age groups are urgently needed. SUMMARY: The use of antiretroviral therapies in older individuals is complex. Development of novel antiretrovirals and antiretroviral combinations with a low propensity for toxicity, drug-drug interactions and reliable pharmacology regardless of age is urgently needed.


BACKGROUND: Weight gain after antiretroviral therapy (ART) initiation is common, but its implication for mortality is unknown. We evaluated weight change in the first year after ART initiation and its association with subsequent mortality. METHODS: Human immunodeficiency virus-infected patients from the Veterans Aging Cohort Study (VACS) who initiated ART between 2000 and 2008, with weight recorded at baseline and 1 year later, were followed another 5 years for mortality. Baseline body mass index (BMI) was classified as underweight (<18.5 kg/m(2)), normal (18.5-24.9 kg/m(2)), overweight (25-29.9 kg/m(2)), and obese (>=30 kg/m(2)). We used multivariable Cox models to assess mortality risk with adjustment for disease severity using the VACS Index. RESULTS: The sample consisted of 4184 men and 127 women with a mean age of 47.9 +/- 10.0 years. After 1 year of ART, median weight change was 5.9 pounds (2.7 kg) (interquartile range, -2.9 to 17.0 pounds, -1.3 to 7.7 kg). Weight gain after ART initiation was associated with lower mortality among underweight and normal-weight patients. A minimum threshold of 10- to 19.9-pound (4.5 to 9.0 kg) weight gain was beneficial for normal-weight patients (hazard ratio, 0.56; 95% confidence interval, .41-.78), but there was no clear benefit to weight gain for overweight/obese patients. Baseline weight, CD4 cell count status, and hemoglobin level were strongly associated with weight gain. Risk for weight gain was higher among those with greater disease severity, regardless of weight at initiation. CONCLUSIONS: The survival benefits of weight gain after ART initiation are dependent on starting BMI. Weight gain after ART is associated with lower mortality for those who are not initially overweight.


OBJECTIVES: Certain non-AIDS-related diseases have been associated with immunodeficiency and HIV RNA levels in HIV-infected patients on combination antiretroviral therapy (cART). We aimed to investigate these associations in patients not yet on cART, when potential antiretroviral-drug-related effects are absent and variation in
RNA levels is greater. METHODS: Associations between, on the one hand, time-updated CD4 counts and plasma HIV RNA and, on the other hand, a composite non-AIDS-related endpoint, including major cardiovascular diseases, liver fibrosis/cirrhosis, and non-AIDS-related malignancies, were studied with multivariate Poisson regression models in 12,800 patients diagnosed with HIV infection from 1998 onwards while not yet treated with cART. RESULTS: During 18,646 person-years of follow-up, 203 non-AIDS-related events occurred. Compared with a CD4 count \( \geq 500 \) cells/\( \mu L \), adjusted relative risks (RRs) for the composite endpoint were 4.71 [95% confidence interval (CI) 2.98-7.45] for a CD4 count < 200 cells/\( \mu L \), 2.06 (95% CI 1.38-3.06) for a CD4 count of 200-349 cells/\( \mu L \), and 1.19 (95% CI 0.82-1.74) for a CD4 count of 350-499 cells/\( \mu L \). There was no evidence for an independent association with HIV RNA. Other important covariates were age [RR 1.40 (95% CI 1.31-1.49) per 5 years older], hepatitis B virus coinfection [RR 5.66 (95% CI 3.87-8.28)] and hepatitis C virus coinfection [RR 9.26 (95% CI 6.04-14.2)]. CONCLUSIONS: In persons not yet receiving cART, a more severe degree of immunodeficiency rather than higher HIV RNA levels appears to be associated with an increased risk of our composite non-AIDS-related endpoint. Larger studies are needed to address these associations for individual non-AIDS-related events.

Other


BACKGROUND AND OBJECTIVE: The objective of this study was to analyze the deaths caused by non-AIDS diseases in a cohort of HIV-infected patients treated between 1998 and 2011. PATIENTS AND METHODS: Information on the causes of death was collected retrospectively, and then classified according to the deaths code (CoDe) algorithm. Patient characteristics and causes of death were compared for two periods: 1998-2004 and 2005-2011. RESULTS: A total of 159 out of the 1070 patients cared for in study period died, 56 (35%) due to AIDS events and 86 (54%) due to non-AIDS events (NAEs); in 17 (11%) the cause of death could not be determined. Overall, the main causes of death were infections (32%), cancer (17%), and unnatural deaths (17%). There was lower mortality from AIDS-related conditions during the second period (18.5% vs 47%; \( P<.001 \)) and higher mortality from NAEs (68% vs 45%; \( P=.006 \)). There was a very sharp increase in non-AIDS-defining cancers (18.5% vs 2.1%, \( p=001 \)), and increased deaths from cardiovascular disease (9.2% vs 2.1%, \( P=.06 \)). Patients who died in the second period were older, and had a better immunological and virological status at cohort entry and before death. They received antiretroviral therapy (ART) more often and were more often virologically suppressed before death (61.5% vs 24%; \( P=.001 \)). CONCLUSIONS: Non-AIDS-defining cancers, unnatural deaths, and cardiovascular diseases are now major causes of death in patients with HIV. In recent years the majority of deceased patients are on ART and with virological suppression.


BACKGROUND: Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF; Stribild((R))) is a guideline-recommended regimen for HIV treatment-naive patients and a switch option for virologically suppressed patients. OBJECTIVE: The purpose of this analysis was to understand how HIV patients' symptoms change after switching to Stribild((R)) versus continuing a regimen consisting of a non-nucleoside...
reverse transcriptase inhibitor (NNRTI) with emtricitabine and tenofovir disoproxil fumarate. METHODS: A secondary analysis was conducted of the STRATEGY-NNRTI study (GS-US-236-0121), a randomized, open-label, phase IIib trial of HIV-infected adults who were taking an NNRTI plus FTC/TDF and were randomly assigned (2:1) either to Stribild(R) ('switch') or to continue on their existing regimen ('no-switch'). Logistic regressions and longitudinal modeling were conducted to evaluate the relationship of treatment with bothersome symptoms. These models adjusted for age, sex, race, number of bothersome symptoms at baseline, Veterans Aging Cohort Study Risk (VACS) Index score, years since HIV diagnosis, and first antiretroviral therapy use, NNRTI type, serious mental illness, and baseline depression and health-related quality of life (HRQL) scores. RESULTS: At baseline, the prevalence of nightmares, vivid dreams, weird/intense dreams, muscle aches/joint pain, and fevers/chills/sweats was greater in the switch group. The prevalence of nightmare, vivid dreams, weird/intense dreams, dizzy/lightheadedness, fatigue/loss of energy, and pain/numbness/tingling in hands/feet deceased in the switch group at week 4, and these benefits were maintained over time. Nervous/anxious, drowsiness, trouble remembering, off balance, and body changes decreased in the switch group at week 4 but were not maintained over time. Difficulty sleeping, diarrhea/loose bowels, and bloating did not differ in prevalence at week 4 or 48, but longitudinal models suggested differences between groups over time. HRQL did not differ between groups and was unchanged over time. CONCLUSIONS: In this study sample, a switch to co-formulated EVG/COBI/FTC/TDF was associated with significant persistent improvements in six patient-reported HIV symptoms.


This paper examines how care-giving to adults and/or children and care-receiving is associated with the health and wellbeing of older people aged 50+ in rural South Africa. Data used are from a cross-sectional survey adapted from World Health Organization's Study on Global Ageing and Adult Health (SAGE) conducted in 2009/10 in rural South Africa. Bivariate statistics and multivariate logistical regression were used to assess the relationship between care-giving and/or care-receiving with functional disability, quality of life or emotional wellbeing, and self-rated health status, adjusted for socio-demographic factors. Sixty-three per cent of 422 older people were care-givers to at least one young adult or child; 27 per cent of older people were care-givers due to HIV-related reasons in young adults; 84 per cent of participants were care-recipients mainly from adult children, grandchildren and spouse. In logistic regressions adjusting for sex, age, marital status, education, receipt of grants, household headship, household wealth and HIV status, care-giving was statistically significantly associated with good functional ability as measured by ability to perform activities of daily living. This relationship was stronger for older people providing care-giving to adults than to children. In contrast, care-givers were less likely to report good emotional wellbeing; again the relationship was stronger for care-givers to adults than children. Simultaneous care-giving and -receiving was likewise associated with good functional ability, but about a 47 per cent lower chance of good emotional wellbeing. Participants who were HIV-infected were more likely to be in better health but less likely to be receiving care than those who were HIV-affected. Our findings suggest a strong relationship between care-giving and poor emotional wellbeing via an economic or psychological stressor pathway. Interventions that improve older people's socio-economic circumstances and reduce financial hardship as well as those that provide social support would go some way towards mitigating this relationship.


BACKGROUND: Our aim was to assess internal consistency reliability, construct validity, and test-retest reliability of the HDQ with adults living with HIV in Canada and Ireland. METHODS: We recruited adults 18 years of
We administered the HDQ paired with reference measures (World Health Organization Disability Assessment Schedule, SF-36 Questionnaire, Medical Outcomes Study Social Support Survey), and a demographic questionnaire. We calculated HDQ disability presence, severity and episodic scores (scored from 0-100). We calculated Cronbach’s alpha and Intraclass Correlation Coefficients (ICC) (Canada only) for the disability severity and episodic scores and considered coefficients >0.80 and >0.70 as acceptable, respectively. To assess construct validity, we tested 40 a priori hypotheses of correlations between scores on the HDQ and reference measures and two known group hypotheses comparing HDQ presence and severity scores based on age and comorbidity. We considered acceptance of at least 75% of hypotheses as demonstrating support for construct validity. RESULTS: Of the 235 participants (139 Canada; 96 Ireland), the majority were men (74% Ireland; 82% Canada) and were taking antiretroviral therapy (88% Ireland; 91% Canada). Compared with Irish participants, Canadian participants were older (median age: 48 versus 41 years) and reported living with a higher median number of comorbidities (4 versus 1). Cronbach’s alpha for Irish and Canadian participants were 0.97 (95% confidence interval (CI): 0.97-0.98) and 0.96 (95% CI: 0.95-0.98), respectively, for the severity scale and 0.98 (95% CI: 0.97-0.98) and 0.96 (95% CI: 0.95-0.98), respectively, for the episodic scale. Of the 40 construct validity correlation hypotheses, 32 (80%) and 22 (55%) were supported among the Canadian and Irish samples respectively; both (100%) known group hypotheses were also supported. ICC values for Canadian participants ranged from 0.80 (95% CI: 0.71, 0.86) in the cognitive domain to 0.89 (95% CI: 0.83, 0.92) in the social inclusion domain. CONCLUSIONS: The HDQ demonstrates internal consistency reliability and a variable degree of construct validity when administered to adults living with HIV in Canada and Ireland. The HDQ demonstrates test-retest reliability when administered to adults with HIV in Canada. Further validation of the HDQ outside of Canada is needed.

Organ transplantation is an acceptable option for human immunodeficiency virus (HIV)-infected patients with end-stage kidney or liver disease. With worse outcomes on the waitlist, HIV-infected patients may actually be disproportionately affected by the organ shortage in the United States. One potential solution is the use of HIV-infected deceased donors (HIVDD), recently legalized by the HIV Organ Policy Equity (HOPE) Act. This is the first analysis of patient-specific data from potential HIVDD, retrospectively examining charts of HIV-infected patients dying in care at six HIV clinics in Philadelphia, Pennsylvania from January 1, 2009 to June 30, 2014. Our data suggest that there are four to five potential HIVDD dying in Philadelphia annually who might yield two to three kidneys and three to five livers for transplant. Extrapolated nationally, this would approximate 356 potential HIVDD yielding 192 kidneys and 247 livers annually. However, several donor risk indices raise concerns about the quality of kidneys that could be recovered from HIVDD as a result of older donor age and comorbidities. On the other hand, livers from these potential HIVDD are of similar quality to HIV-negative donors dying locally, although there is a high prevalence of positive hepatitis C antibody.

BACKGROUND: Avahan, a large-scale HIV prevention program in India, transitioned over 130 intervention sites from donor funding and management to government ownership in three rounds. This paper examines the transition experience from the perspective of the communities targeted by these interventions. METHODS: Fifteen qualitative longitudinal case studies were conducted across all three rounds of transition, including 83 in-depth interviews and 45 focus group discussions. Data collection took place between 2010 and 2013 in four states: Andhra Pradesh, Maharashtra, Karnataka, and Tamil Nadu.
Pradesh, Karnataka, Maharashtra and Tamil Nadu. RESULTS: We find that communication about transition was difficult at first but improved over time, while issues related to employment of peer educators were challenging throughout the transition. Clinical services were shifted to government providers resulting in mixed experiences depending on the population being targeted. Lastly, the loss of activities aimed at community ownership and mobilization negatively affected the beneficiaries' view of transition. CONCLUSIONS: While some programmatic changes resulted in improvements, additional opportunity costs for beneficiaries may pose barriers to accessing HIV prevention services. Communicating and engaging community stakeholders early on in future such transitions may mitigate negative feelings and lead to more constructive relationships and dialogue.


The CDC estimates that in 2015, half of all people living with HIV in the U.S. will be over age 50. Older adults remain sexually active and 16% of all new HIV diagnoses occur in adults 50 and older. However, older adults rarely see themselves at risk for HIV/AIDS and physicians are frequently reluctant to discuss sex. To address the issue of aging and HIV, ACRIA created its National Older Adults with HIV (NOAH) technical assistance and capacity building program. NOAH targets aging and HIV providers that serve older adults at risk for or living with HIV. Program goals include increasing knowledge, reducing stigma, and creating partnerships between senior service providers (SSPs) and HIV service providers. In its first four years NOAH training was provided to 150 organizations in eight cities across the U.S., reaching 332 agency staff. Outcome evaluation found significant increases in knowledge about HIV and aging, and programmatic impact with regard to integration of older adults and HIV information in participating agencies' activities. Ongoing issues included recruiting SSPs and difficulties in reaching agencies that participated for short- and long-term follow-up. Implications for workforce development are discussed.


BACKGROUND: Because of health disparities, incarcerated persons are at higher risk for multiple health issues, including HIV. Correctional facilities have an opportunity to provide HIV services to an underserved population. This article describes Centers for Disease Control and Prevention (CDC)-funded HIV testing and service delivery in correctional facilities. METHODS: Data on HIV testing and service delivery were submitted to CDC by 61 health department jurisdictions in 2013. HIV testing, HIV positivity, receipt of test results, linkage, and referral services were described, and differences across demographic characteristics for linkage and referral services were assessed. Finally, trends were examined for HIV testing, HIV positivity, and linkage from 2009 to 2013. RESULTS: Of CDC-funded tests in 2013 among persons 18 years and older, 254,719 (7.9%) were conducted in correctional facilities. HIV positivity was 0.9%, and HIV positivity for newly diagnosed persons was 0.3%. Blacks accounted for the highest percentage of HIV-infected persons (1.3%) and newly diagnosed persons (0.5%). Only 37.9% of newly diagnosed persons were linked within 90 days; 67.5% were linked within any time frame; 49.7% were referred to partner services; and 45.2% were referred to HIV prevention services. There was a significant percent increase in HIV testing, overall HIV positivity, and linkage from 2009 to 2013. However, trends were stable for newly diagnosed persons. CONCLUSIONS: Identification of newly diagnosed persons in correctional facilities has remained stable from 2009 to 2013. Correctional facilities seem to be reaching blacks, likely due to higher incarceration rates. The current findings indicate that improvements are needed in HIV testing strategies, service delivery during incarceration, and linkage to care postrelease.

BACKGROUND: The objectives are to examine disparities in all-cause mortality risk among HIV-positive Latinos with injection drug use (IDU) history, and to identify individual- and neighborhood-level predictors. METHODS: Florida surveillance data for persons diagnosed with HIV 2000-2008 were merged with 2007-2011 administrative data from the American Community Survey. Hazard ratios (HR) were calculated using multi-level weighted Cox regression adjusting for individual and neighborhood (ZCTA-level) factors. RESULTS: Of 10,989 HIV-positive Latinos, 10.3% had IDU history. Latinos with IDU history were at increased mortality risk compared with Latinos without IDU history after controlling for individual and neighborhood factors (adjusted HR [aHR] 1.61, 95% confidence interval [CI] 1.43-1.80). Factors associated with mortality for those with IDU history included: being 40-59 (aHR 6.48, 95% CI 1.41-121.05) and >/=60 years (aHR 18.75, 95% CI 3.83-356.45) compared with 13-19 years of age; being diagnosed with AIDS within 3 months of HIV (aHR 2.31, 95% CI 1.87-2.86); residing in an area with >/=50% Latinos compared with <25% Latinos (aHR 1.56, 95% CI 1.19-2.04); and residing in a rural compared with an urban area at the time of diagnosis (aHR 1.73, 95% CI 1.06-2.70). Race and neighborhood poverty were not predictors among those with IDU, but were among those without. CONCLUSION: HIV-positive Latinos with IDU history are at increased mortality risk and have unique contributing factors. Tertiary prevention strategies should target those who are older, diagnosed at later stages, and those who live in predominantly Latino and rural areas.


The progressively older population in developed countries is reflected in an increase in the number of people suffering from age-related chronic inflammatory diseases such as metabolic syndrome, diabetes, heart and lung diseases, cancer, osteoporosis, arthritis, and dementia. The heterogeneity in biological aging, chronological age, and aging-associated disorders in humans have been ascribed to different genetic and environmental factors (i.e., diet, pollution, stress) that are closely linked to socioeconomic factors. The common denominator of these factors is the inflammatory response. Chronic low-grade systemic inflammation during physiological aging and immunosenescence are intertwined in the pathogenesis of premature aging also defined as ‘inflammaging.’ The latter has been associated with frailty, morbidity, and mortality in elderly subjects. However, it is unknown to what extent inflammaging or longevity is controlled by epigenetic events in early life. Today, human diet is believed to have a major influence on both the development and prevention of age-related diseases. Most plant-derived dietary phytochemicals and macro- and micronutrients modulate oxidative stress and inflammatory signaling and regulate metabolic pathways and bioenergetics that can be translated into stable epigenetic patterns of gene expression. Therefore, diet interventions designed for healthy aging have become a hot topic in nutritional epigenomic research. Increasing evidence has revealed that complex interactions between food components and histone modifications, DNA methylation, non-coding RNA expression, and chromatin remodeling factors influence the inflammaging phenotype and as such may protect or predispose an individual to many age-related diseases. Remarkably, humans present a broad range of responses to similar dietary challenges due to both genetic and epigenetic modulations of the expression of target proteins and key genes involved in the metabolism and distribution of the dietary constituents. Here, we will summarize the epigenetic actions of dietary components, including phytochemicals, and macro- and micronutrients as well as metabolites, that can attenuate inflammaging. We will discuss the challenges facing personalized nutrition to translate highly variable interindividual epigenetic diet responses to potential individual health benefits/risks related to aging disease.

The impact of age and physical health on processing speed was investigated in 42 non-demented HIV+ individuals ranging in age from 30 to 75. We used the Medical Outcomes Study-HIV Healthy Survey (MOS-HIV) to measure self-reported physical health, neuropsychological tests to measure psychomotor and cognitive processing speed (Delis-Kaplan Executive Function System Trail Making Test, Grooved Pegboard Test, letter and category fluency), and a test of the foreperiod effect to measure reaction time under increasing attentional load. Results indicated that aging and worse physical health each independently contributed to slowing on different processing speed measures, while the interaction between aging and physical health did not contribute to processing speed. These findings highlight the importance of considering physical health separately from age when measuring cognitive function in HIV+ adults.


Within the areas of literature on both population aging and health and homelessness, little attention has been given to the opportunities and barriers to healthy aging among older persons with a history of homelessness. Set in the context of inner-city Toronto, Canada, this article reports on the findings from qualitative interviews with 29 formerly homeless older persons. The findings illustrate participants’ experiences of positive health change since moving into a stable housing environment and the aspects of housing they perceive to have improved their health and wellbeing. The qualitative findings also draw attention to the ongoing barriers to healthy aging that can be experienced among older persons with a history of homelessness. Overall, this study draws on the lived experiences of formerly homeless older persons to offer a better understanding of the long-term effects of homelessness on health, wellbeing, and aging.


OBJECTIVE: Food insecurity may be a modifiable and independent risk factor for worse control of medical conditions, but it has not been explored among veterans. We determined the prevalence of, and factors independently associated with, food insecurity among veterans in the Veterans Aging Cohort Study (VACS). METHODS: Using data from VACS from 2002-2008, we determined the prevalence of food insecurity among veterans who have accessed health care in the Veterans Health Administration (VA) as defined by "concern about having enough food for you or your family in the past month." We used multivariable logistic regression to determine factors independently associated with food insecurity and tests of trend to measure the association between food insecurity and control of hypertension, diabetes, HIV, and depression. RESULTS: Of the 6,709 veterans enrolled in VACS, 1,624 (24%) reported being food insecure. Food insecurity was independently associated with being African American, earning <$25,000/year, recent homelessness, marijuana use, and depression. Being food insecure was also associated with worse control of hypertension, diabetes, HIV, and depression (p<0.001). CONCLUSION: Food insecurity is prevalent and associated with worse control of medical conditions among veterans who have accessed care in the VA.
BACKGROUND: Weight gain after antiretroviral therapy (ART) initiation is common, but its implication for mortality is unknown. We evaluated weight change in the first year after ART initiation and its association with subsequent mortality. METHODS: Human immunodeficiency virus-infected patients from the Veterans Aging Cohort Study (VACS) who initiated ART between 2000 and 2008, with weight recorded at baseline and 1 year later, were followed another 5 years for mortality. Baseline body mass index (BMI) was classified as underweight (<18.5 kg/m²), normal (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), and obese (≥30 kg/m²). We used multivariable Cox models to assess mortality risk with adjustment for disease severity using the VACS Index. RESULTS: The sample consisted of 4184 men and 127 women with a mean age of 47.9 ± 10.0 years. After 1 year of ART, median weight change was 5.9 pounds (2.7 kg) (interquartile range, -2.9 to 17.0 pounds, -1.3 to 7.7 kg). Weight gain after ART initiation was associated with lower mortality among underweight and normal-weight patients. A minimum threshold of 10-19.9-pound (4.5 to 9.0 kg) weight gain was beneficial for normal-weight patients (hazard ratio, 0.56; 95% confidence interval, .41-.78), but there was no clear benefit to weight gain for overweight/obese patients. Baseline weight, CD4 cell count status, and hemoglobin level were strongly associated with weight gain. Risk for weight gain was higher among those with greater disease severity, regardless of weight at initiation. CONCLUSIONS: The survival benefits of weight gain after ART initiation are dependent on starting BMI. Weight gain after ART is associated with lower mortality for those who are not initially overweight.