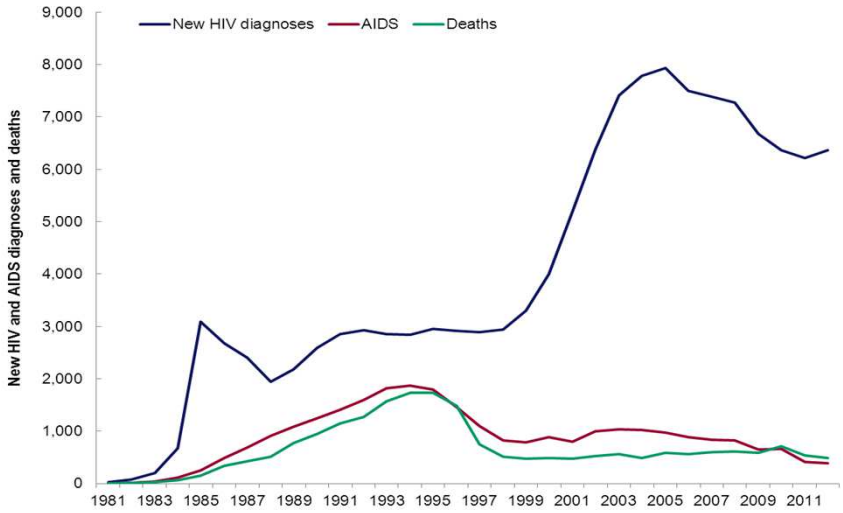
Forget me not: providing care for people living with HIV and dementia (What does the future hold for our elderly HIV patients?)

Dr Simon Rackstraw FRCP
Medical Director, Mildmay Hospital, London
Consultant HIV Physician, Bartshealth NHS Trust, London

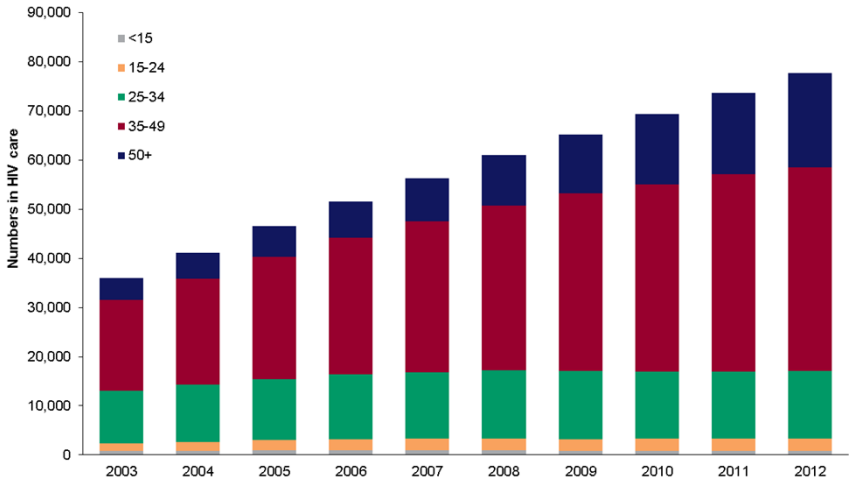
Public Health England

Annual new HIV and AIDS diagnoses and deaths: UK, 1981-2012



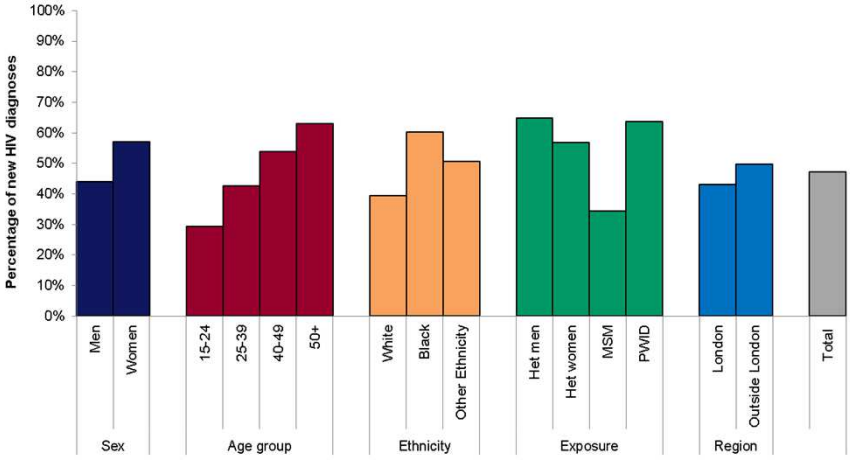
Public Health England

Trends in people diagnosed with HIV accessing care by age group: UK, 2003 – 2012



Public Health England

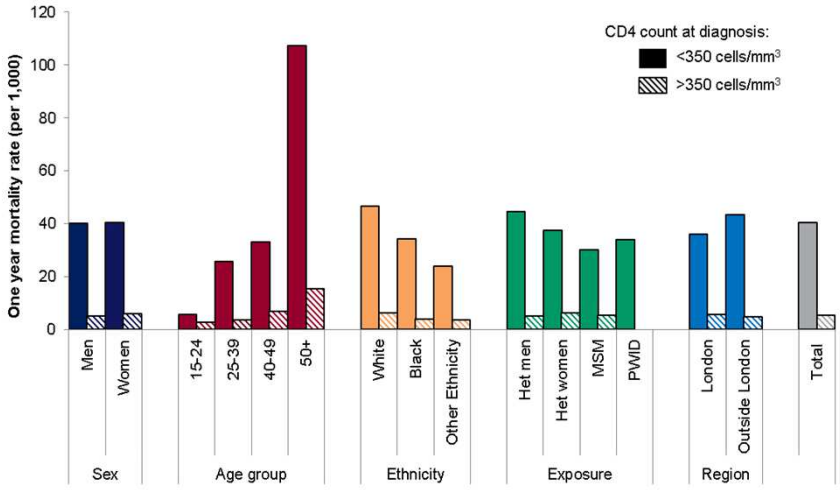
Attributes of late* HIV diagnosis, UK 2012



* CD4 <350 cells/mm^3 within three months of diagnosis

Public Health England

One year mortality among adults diagnosed by CD4 count at diagnosis: UK, 2010

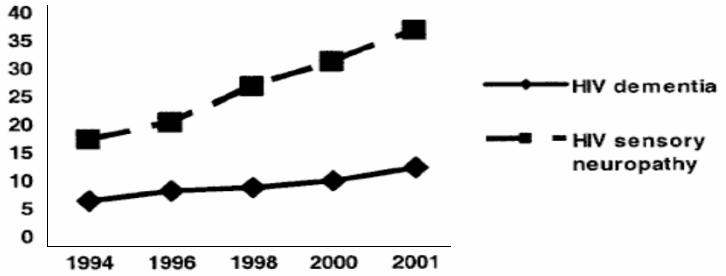


CDC definition of HIV encephalopathy (dementia)

- Clinical findings of disabling cognitive or motor dysfunction interfering with occupation or activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings.
- Methods to rule out such concurrent illness and conditions must include cerebrospinal fluid examination and either brain imaging (computed tomography or magnetic resonance) or autopsy.

1987 Revision of the CDC Surveillance Case definition for Acquired Immunodeficiency syndrome

Changing epidemiology rising prevalence of HIV dementia



Due to improved survival rates, the cumulative prevalence of HIV dementia has risen

Adapted from McArthur J, et al, J. Neurovirology 2003;9:205-221

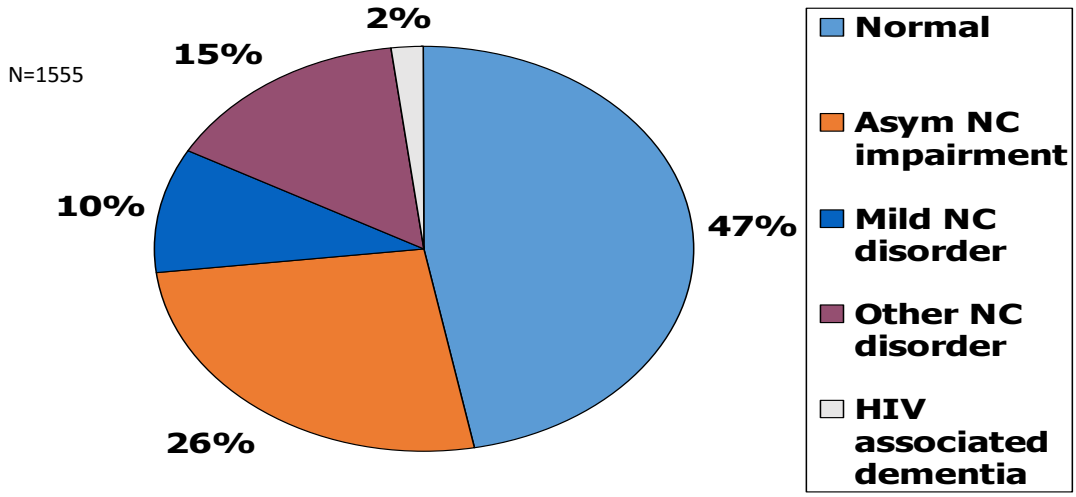
"Frascati" definition of HIV Associated Neurocognitive Disorder (HAND)

	No Pre-existing Cause	Delirium Absent	Acquired Impairment in ≥ 2 Cognitive Abilities	Interferes with Daily Functioning
Asymptomatic Neurocognitive Impairment (ANI)	Yes	Yes	Yes (>1SD)	No
Mild Neurocognitive Disorder (MND)	Yes	Yes	Yes (>1SD)	Mild
HIV-Associated Dementia (HAD)	Yes	Yes	Marked (>2SD)	Marked

Cognitive domains: attention-information processing, language, abstraction-executive, complex perceptual motor skills, memory, including learning and recall, simple motor skills or sensory perceptual abilities

Antinori et al, Neurology 2007, 69:1789-99

CHARTER: **C**NS **H**IV **A**nti**R**etroviral **T**herapy **E**ffects **R**esearch Project, Years 2003-2007



Heaton RK et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. Neurology. 2010 Dec 7;75(23):2087-96.

Cognitive impairment in UK MSM

TABLE 2. Estimates of Prevalence of Neurocognitive Impairment in HIV-Positive and HIV-Negative Men

	All Participants			Excluding Participants With Severe Depressive Symptoms		
	HIV-Positive MSM (N = 248)	HIV-Negative MSM (N = 45)	*P*	HIV-Positive MSM (N = 231)	HIV-Negative MSM (N = 44)	*P*
NCI by Frascati criteria, n (%)*			0.32†			0.27†
ANI	34 (13.7)	11 (24.4)		32 (13.9)	11 (25.0)	
MND	16 (6.5)	2 (4.4)		14 (6.1)	2 (4.6)	
HAD	2 (0.8)	0		2 (0.9)	0	
Self-reported functional impairment caused by cognitive difficulties, n (%)			0.007†			0.008†
Mild (2–3 ADL)	38 (15.3)	5 (11.1)		35 (15.2)	4 (9.1)	
Significant (≥4 ADL)	34 (13.7)	0		27 (11.7)	0	
GDS for 5 domains, median (IQR)	0.2 (0–0.6)	0.2 (0–0.8)	0.71	0.2 (0–0.6)	0.2 (0–0.9)	0.75
NCI by GDS for 5 domains, n (%)	78 (31.5)	12 (26.7)	0.52	72 (31.2)	12 (27.3)	0.61
GDS for 10 test scores, median (IQR)	0.3 (0.1–0.8)	0.3 (0.1–0.6)	0.77	0.3 (0.1–0.7)	0.3 (0.1–0.8)	0.78
NCI by GDS for 10 test scores, n (%)	100 (40.3)	19 (42.2)	0.81	92 (39.8)	19 (43.2)	0.68

*For the purposes of applying Frascati criteria to HIV-negative participants, HIV status is ignored.
†Test for trend.
IQR, interquartile range; MND, mild neurocognitive disorder.

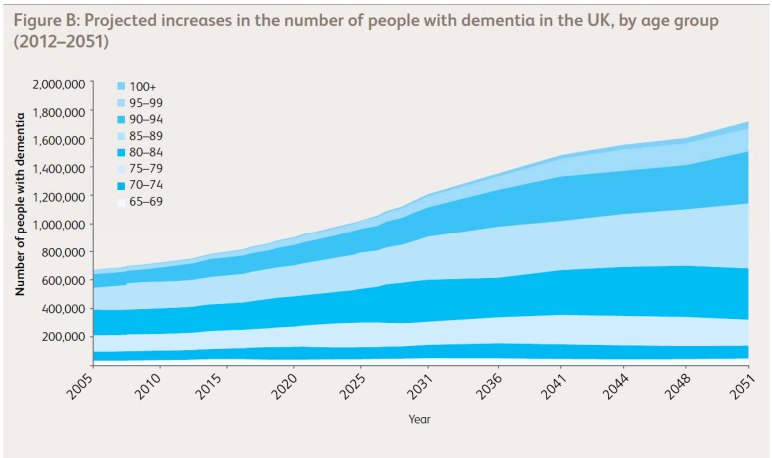
McDonnell J et al. Minimal cognitive impairment in UK HIV-positive men who have sex with men: effect of case definitions and comparison with the general population and HIV-negative men. J Acquir Immune Defic Syndr. 2014 Oct 1;67(2):120-7

Clinical features of HAND: functional impairment

- Activities of daily living
  - Medication adherence[1]
  - Driving (2–3 times as likely to fail tests)[2]
  - Household finances
  - Meal preparation
- Vocational functioning[3]
  - 5 times more likely to complain of job performance problems
  - Twice as likely to be unemployed

1. Andrade AS, et al. Clin Infect Dis 2005;41(6):875–82
2. Marcotte TD, et al. Neurology 2004;63(8):1417–22
3. Heaton RK, et al. Psychosom Med 1994;56:8–17

Projected numbers with dementia in UK



Alzheimer's Society. Dementia in the UK – Update (2014)

Alzheimer's disease

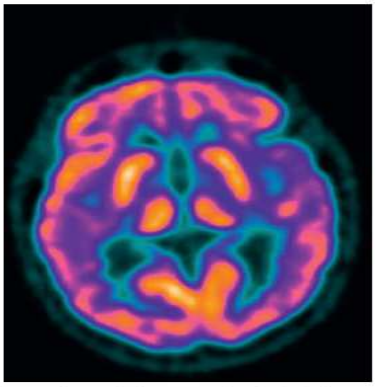


Fig. 1. Positron emission tomography of the brain. Hypometabolism, which appears as the color blue, was demonstrated in the parietal and temporal cortices and is consistent with Alzheimer's disease. Normal metabolic activity, which appears as the color orange, was observed in the frontal cortices and subcortical structures (basal ganglia and thalami). These findings do not support the presence of HIV-associated dementia, which would be expected to show reduced metabolic activity in subcortical regions.

- First report of a combination of Alzheimer's disease and HIV related cognitive impairment in the same patient.

Brousseau KM et al. Dementia with features of Alzheimer's disease and HIV-associated dementia in an elderly man with AIDS. *AIDS* 2009, 23:1029–1031

Cohen *et al. Alzheimer's Research & Therapy* (2015) 7:37
DOI 10.1186/s13195-015-0123-4

alzheimer's research&therapy

REVIEW Open Access

HIV effects on age-associated neurocognitive dysfunction: premature cognitive aging or neurodegenerative disease?

Ronald A Cohen[1*], Talia R Seider[1,2] and Bradford Navia[3]

Table 1 Summary of neurocognition, neuroimaging, neuropathology, and pathophysiology of brain disturbances in HIV and Alzheimer's disease

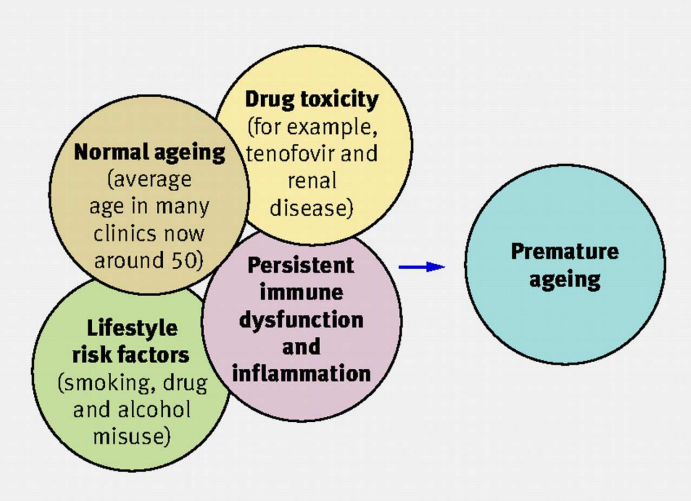
	HIV	Alzheimer's disease	Both
Neurocognitive manifestations	Psychomotor slowing	Primary amnestic disturbance	Memory disturbances
	Executive dysfunction	Anomia	
	Selective cognitive impairments	Global cognitive dysfunction	
Cerebral volumetric changes	Early declines in basal ganglia and frontal lobe volumes	Greater cortical atrophy and ventricular enlargement	Early white matter changes

New comorbidities in the era of HAART

- Cardiovascular disease[1,2,3,4]
- Diabetes mellitus & insulin resistance[4]
- Cancer[5]
- Osteopenia & osteoporosis[6,7]
- Liver failure[8]
- Kidney failure[9]
- Cognitive decline & dementia[10]
- Frailty[11]

1. Klein et al. Do protease inhibitors increase the risk for coronary heart disease in patients with HIV-1 infection? J Acquir Immune Defic Syndr. 2002 Aug 15;30(5):471-7.
2. Hsue et al. Progression of atherosclerosis as assessed by carotid intima-media thickness in patients with HIV infection. Circulation. 2004 Apr 6;109(13):1603-8.
3. Mary-Krause et al. Increased risk of myocardial infarction with duration of protease inhibitor therapy in HIV-infected men. AIDS. 2003 Nov 21;17(17):2479-86
4. Grinspoon et al. State of the science conference: Initiative to decrease cardiovascular risk and increase quality of care for patients living with HIV/AIDS: executive summary. Circulation. 2008 Jul 8;118(2):198-210.
5. Patel et al. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003. Annals of Internal Medicine. 2008.10:728-736.
6. Triant et al. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab. 2008 Sep;93(9):3499-504.
7. Arnsten et al. Decreased bone mineral density and increased fracture risk in aging men with or at risk for HIV infection. AIDS. 2007 Mar 12;21(5):617-23.
8. Bica et al. Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. Clin Infect Dis. 2001 Feb 1;32(3):492-7
9. Odden et al. Cystatin C level as a marker of kidney function in human immunodeficiency virus infection: the FRAM study. Arch Intern Med. 2007 Nov 12;167(20):2213-9.
10. McCutchan et al. HIV suppression by HAART preserves cognitive function in advanced, immune-reconstituted AIDS patients. AIDS. 2007 May 31;21(9):1109-17.
11. Desquilbet et al. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. J Gerontol A Biol Sci Med Sci. 2007 Nov;62(11):1279-86

Ageing and HIV



Deeks, S. G et al. BMJ 2009;338:a3172

Quality and Outcomes

PREVENTION

Impact of Clinical and Therapeutic Factors on Incident Cardiovascular and Cerebrovascular Events in a Population-Based Cohort of HIV-Infected and Non–HIV-Infected Adults

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Department of Medicine (Tripathi, Winniford), University of Mississippi School of Medicine, Jackson, Mississippi; Department of Epidemiology and Biostatistics (Liese, Zhang), Arnold School of Public Health, University of South Carolina, Columbia, South Carolina; Department of Medicine (Albrecht, Rizvi, Duffus), University of South Carolina School of Medicine, Columbia, South Carolina; Department of Neuropsychiatry and Behavioral, University of South Carolina School of Medicine (Jerrell), Columbia, South Carolina

CT

Background: Cardiovascular and cerebrovascular (CVD) events/diseases are a common cause of non–acquired immunodeficiency syndrome (AIDS)-related mortality in the aging human immunodeficiency virus (HIV)-infected population. The incidence rate and clinical correlates of CVD in people living with HIV/AIDS compared

Clin Cardiol. 2014 Sep;37(9):517-22.

Symptoms and comorbidities in older adults with HIV infection

Figure 5: Other major or long-term illnesses

	Diabetes	High blood pressure	Arthritis	Heart disease	Hepatitis B	Hepatitis C	Neurological condition	Cancer	Other	None	Total
Gay/Bisexual men	19	64	43	26	14	12	47	12	72	94	266
Black African women	3	19	9	3	1	1	1	0	6	7	34
White heterosexuals	5	13	10	2	0	5	7	0	14	8	44
Total (N=410)	27	96	62	31	15	18	55	12	92	109	344

Figures shown refer to numbers not percentages. Multiple responses were possible

Power L et al. A national study of ageing and HIV (50 plus) (2010) Joseph Rowntree Foundation

Hopcroft L et al. *Journal of the International AIDS Society* 2013, **16**:18506
http://www.jiasociety.org/index.php/jias/article/view/18506 | http://dx.doi.org/10.7448/IAS.16.1.18506

JIAS Journal of the International AIDS Society

Research article

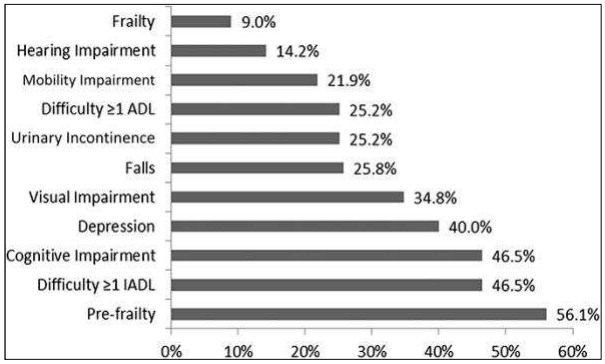
"My body's a 50 year-old but my brain is definitely an 85 year-old": exploring the experiences of men ageing with HIV-associated neurocognitive challenges

Lisa Hopcroft[1], Laura Bester*,[1], Daniel Clement*,[1], Adria Quigley*,[1], Manisha Sachdeva*,[1], Sean B Rourke[2] and Stephanie A Nixon[§,1]

[§]**Corresponding author:** Stephanie A Nixon, Department of Physical Therapy, University of Toronto, 160-500 University Avenue, Toronto, Ontario, Canada M5G 1V7. Tel: +1-416-946-3232. Fax: +1-416-946-8562. (stephanie.nixon@utoronto.ca)
*These authors contributed equally for this work.

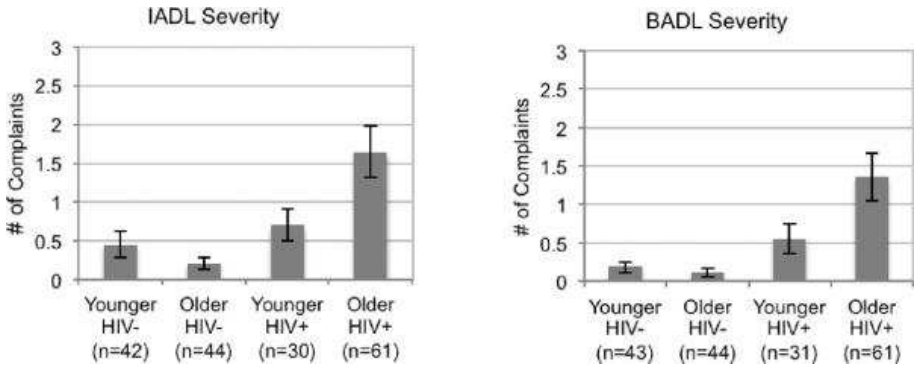
Prevalence of geriatric syndromes

- 155 participants with a median age of 57 (interquartile range: 54–62)
- 94% were men.



Greene et al. Geriatric Syndromes in Older HIV-Infected Adults.
J Acquir Immune Defic Syndr. 2015 Jun 1;69(2):161-7.

Decrease in function in ageing HIV+ patients

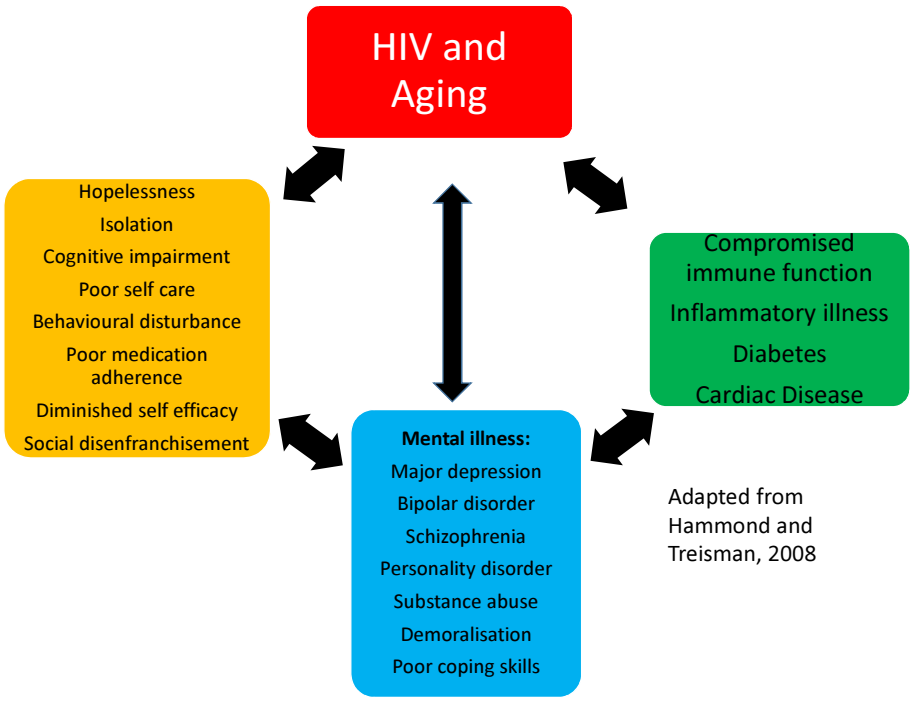


Morgan EE et al. Synergistic effects of HIV infection and older age on daily functioning. J Acquir Immune Defic Syndr. 2012 Nov 1;61(3):341-8.

Ongoing care needs in the era of HAART

- "As people live longer with HAART, there is a rising number of HIV-positive people over 50 years old. They are more likely to have poorer psychological health related to a greater likelihood of comorbid conditions and economic hardship, and of being more severely affected by HIV-related stigma."
- "There has been a shift from acute mental health problems associated with dying to chronic complex problems associated with living."
- "The health of some HIV-positive people does not improve with HAART and some may die. Because of the optimism associated with HAART, failure to respond to the therapy may lead to a profound feeling of failure."

G Green and R Smith. The psychosocial and health care needs of HIV-positive people in the United Kingdom following HAART: a review. HIV Medicine (2004), 5 (Suppl. 1),1–4



Adapted from Hammond and Treisman, 2008

Psychosocial response

- Uncertainty: disability, not death?
- Double diagnoses
- Impact of stigma & discrimination
- Interaction of physical, psychological, and social

Bravo P et al. Tough decisions faced by people living with HIV: a literature review of psychosocial problems. AIDS Rev. 2010 Apr-Jun;12(2):76-88

Attitudes to long term care

Would residential homes or places for the long-term sick have the expertise to be able to look after an older person with HIV ?

52-year-old gay man from Cardiff

I fear hugely going into a home, or getting so frail or ill and I have to be looked after by a paid care agency in my own home, i.e. I fear the attitudes towards HIV that I may find and ignorance from care staff. One of our HIV charity trustees died last year and a private care agency actually refused to provide him with care at home when he was dying of cancer … they did not want to come into contact with his bodily fluids … and if I get dementia … I may not be able to fight this disrespect and stigma or educate them on my care.

57-year-old white heterosexual woman from Cornwall

Power L et al. A national study of ageing and HIV (50 plus) (2010) Joseph Rowntree Foundation

Mildmay Hospital

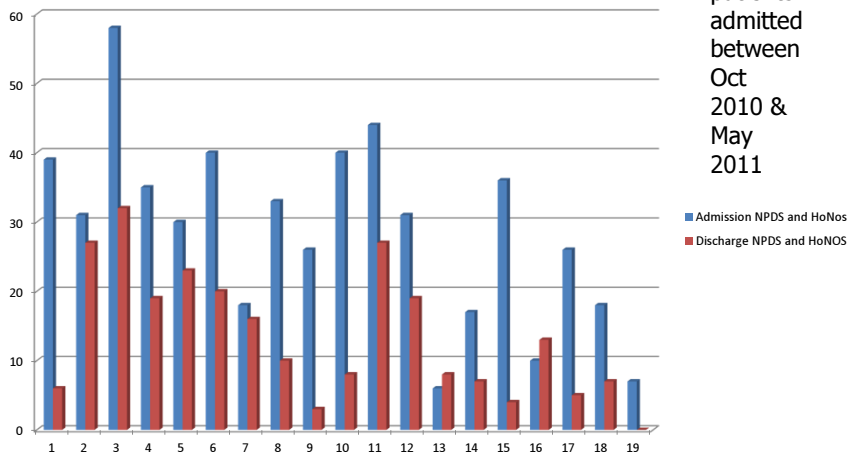
Ageing cohort at the Mildmay

- In year 2005/2006 21% of admissions to Mildmay were 50 years or older
- In the most recent year 2013/2014 37.3% of admissions to Mildmay were 50 years or older
- Current distribution of ages gives a median age of admission of 47

Mildmay Mission hospital admission trends

- Increasing age of patients
- Increasing neurological disability
- Increasing amount of comorbidities
- Increasing numbers of patients loss to follow
- New neurological syndromes i.e CD8 lymphocytosis, CSF escape

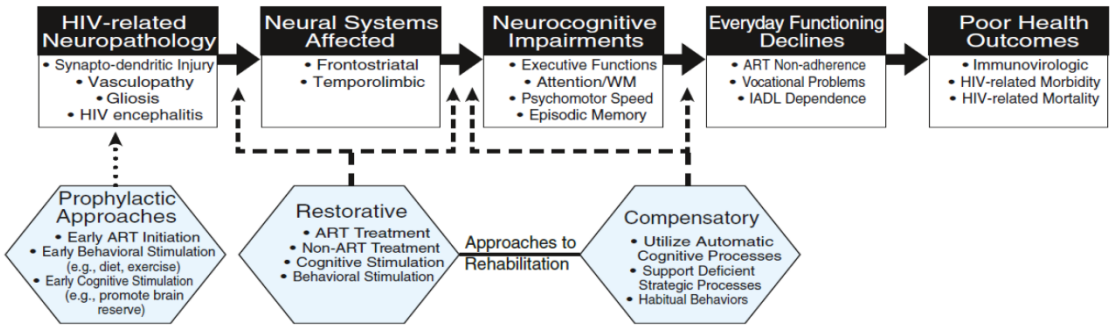
Measuring rehabilitation outcomes - Comparison of Admission and Discharge scores (NPDS & HoNOS-ABI combined)



19 patients admitted between Oct 2010 & May 2011

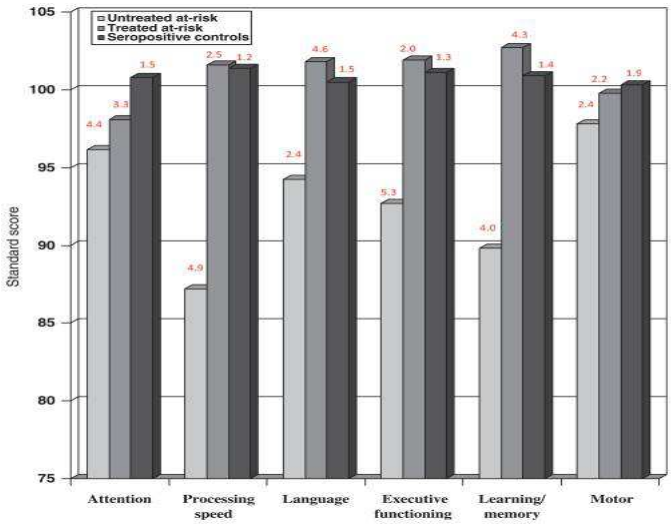
Rackstraw et al. A preliminary investigation of the use of a 'basket' of outcome measures within a rehabilitation service for adults diagnosed with HIV-related neurological disorders. Abstract 5.8, 10th AIDS Impact Conference, Santa Fe, USA; September , 2011

Identification and interventions



Weber E, Blackstone K, Woods SP. Cognitive neurorehabilitation of HIV-associated neurocognitive disorders: a qualitative review and call to action. Neuropsychol Rev. 2013 Mar;23(1):81-98..

Treatment of cerebrovascular risk factors



Foley J et al.Neurocognitive functioning in HIV-1 infection: effects of cerebrovascular risk factors and age. Clin Neuropsychol. 2010 Feb;24(2):265-85.

J. Neurovirol. (2014) 20:233–242
DOI 10.1007/s13365-014-0240-z

An active lifestyle is associated with better neurocognitive functioning in adults living with HIV infection

Pariya L. Fazeli · Steven Paul Woods · Robert K. Heaton · Anya Umlauf · Ben Gouaux · Debra Rosario · Raeanne C. Moore · Igor Grant · David J. Moore · the HNRP Group

Received: 6 September 2013 / Revised: 21 January 2014 / Accepted: 29 January 2014 / Published online: 20 February 2014

Abstract Studies of healthy adults show that engagement in physical, social, and mental activities is associated with better cognitive outcomes, suggesting that these activities may increase cognitive reserve. Given the prevalence and real-world impact of HIV-associated neurocognitive disorders (HAND), the present study examined the association between neurocognitive outcomes and self-reported proxies for physical exercise, social activity, and mental activity (employment was used as a proxy for mental activity) among 139 HIV-infected adults (M_{age} = 48.7; 48 % age 50+). Participants completed a neuromedical and neuropsychological battery and were classified based on the number of self-reported active lifestyle factors (ALFs; 0 to 3), including physical exercise, social activity, and current employment. The association between ALFs and both demographically adjusted average neuropsychological T-scores and HAND diagnoses was examined. Results revealed that an increased number of ALFs were associated with better global neurocognitive performance as well as a lower prevalence of HAND. These cross-sectional findings suggest that an active engagement in life may bolster neurocognitive functioning, perhaps by enhancing cognitive and/or brain reserve. However, an alternative explanation might be that persons with better neurocognitive functioning are more inclined and able to engage in these life activities. Future studies should utilize neuroimaging methodology, longitudinal data, and interventional approaches to establish cause–effect relationships and uncover the neural mechanisms whereby physical, social, and mental stimulation may protect neurocognition via cognitive reserve among those living with HIV.

Keywords Cognitive reserve · NeuroAIDS · Cognitive impairment · Protective factors

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Department of Psychiatry, University of California San Diego, San Diego, CA, USA

D. J. Moore (✉)

Introduction

Infection with HIV continues to negatively impact the central nervous system despite effective combination antiretroviral therapy (cART) that has improved survival rates (Heaton et al. 2011). Although the prevalence of HIV-associated dementia (HAD) has decreased in the cART era, milder forms of HIV-associated neurocognitive disorders (HAND) that nevertheless commonly interfere with real-world functioning are observed in about half of HIV-infected adults (Heaton et al. 2010). With the increased longevity of HIV-infected individuals (Deeks and Phillips 2009) and the potential combined effect of HIV and aging on neurocognition (Cherner et al. 2004; Hardy et al. 1999; Wilkie et al. 2003), there is a significant need to examine factors that may help this high-risk population to potentially avoid, or delay the onset of, neurocognitive impairment. Successful cognitive aging occurs in a subset of persons living with HIV and is associated with better everyday functioning (Malaspina et al. 2011), so isolating factors that may further explain the heterogeneity in neurocognitive trajectories in this population is warranted.

Among both HIV-infected and uninfected adults, research to date has shown that higher education, better socioeconomic status, a more cognitively challenging occupation, and a higher intelligence quotient (IQ) are associated with better

e D et al. Speed of Processing Training with Middle-Age and Older Adults HIV: A Pilot Study. J Assoc Nurses AIDS Care. 2012 Nov; 23(6): 500–510.