HIV and Ageing
– A Focus on Co-Morbidities and Non-pharmacological Interventions

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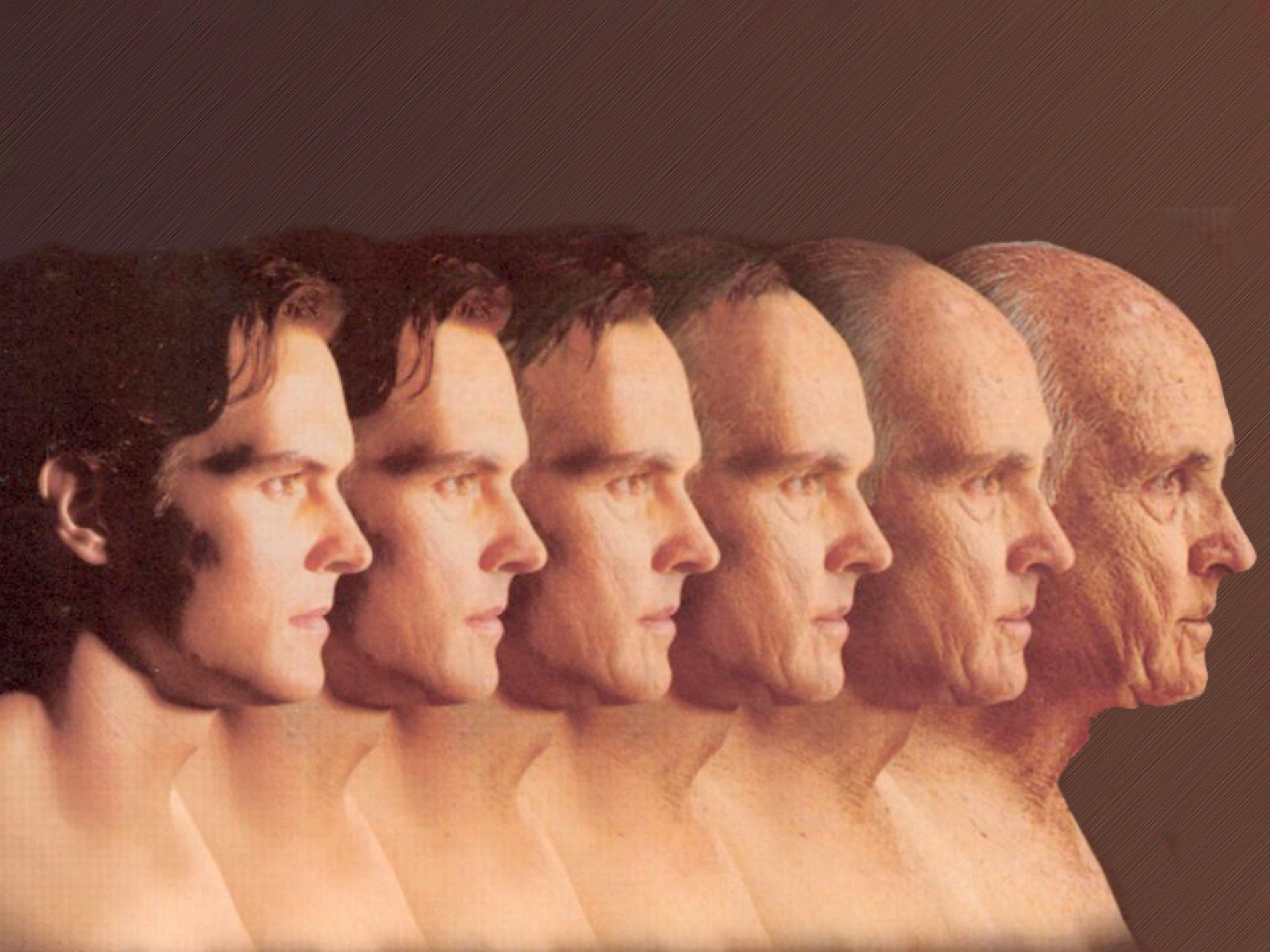
2nd International Forum on HIV & Rehabilitation Research
CUHRRC & RHIVA Meeting
October 11th 2014

CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

British HIV Association
BHIVA

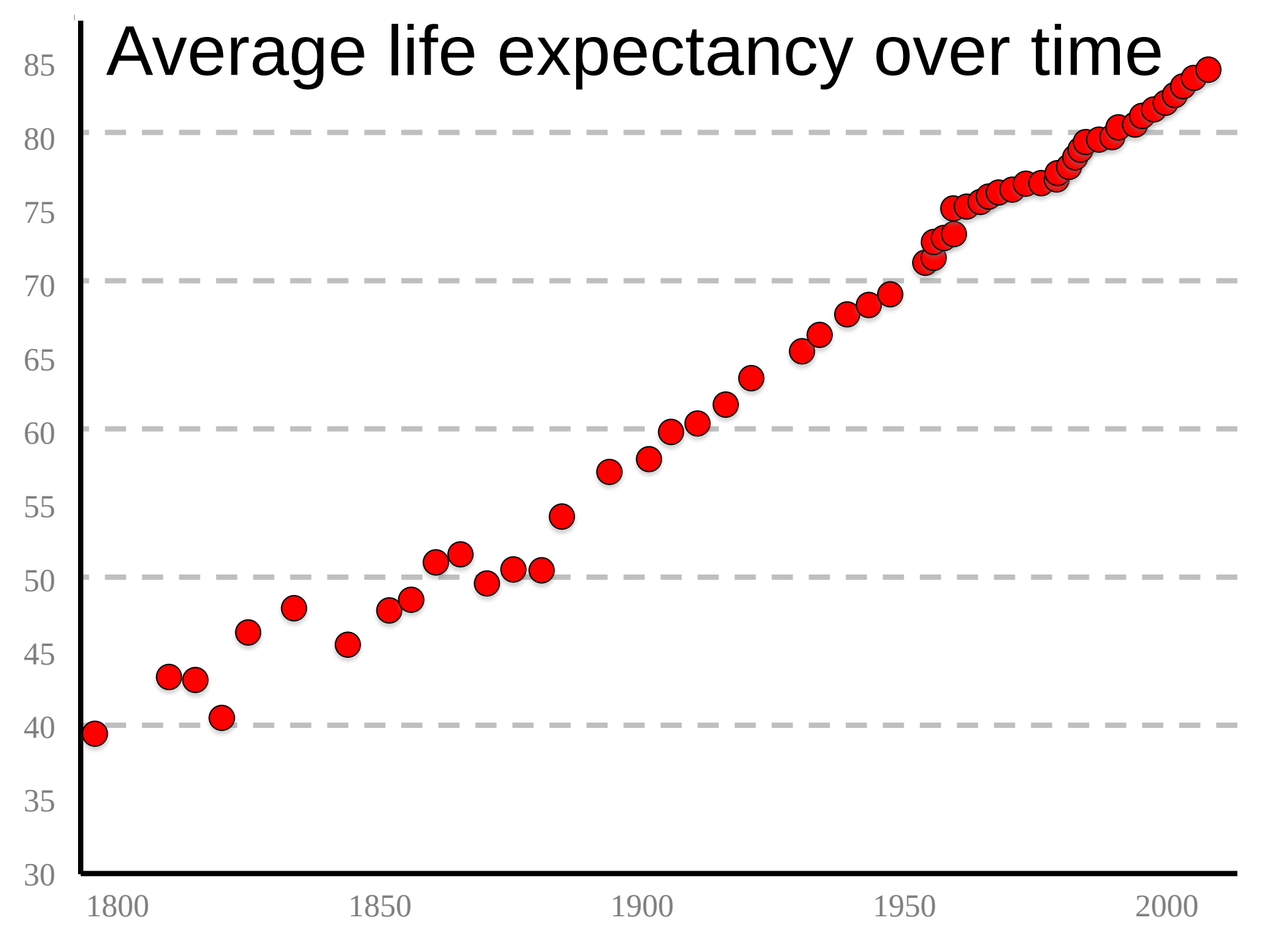
HIV and Ageing

- Ageing
  - General trends
- HIV-related
  - Disease-related prognosis
  - Disease-related & disease-associated factors
- Interventions
  - Nutritional
  - Cardiovascular risk interventions
  - Bone health
  - **Exercise**
  - “Socialisation”



Ban Ki-Moon - UN Secretary General, 2012

People are living longer …
For most of human history only 3-4% >65 yrs


Average life expectancy over time
85
80
75
70
65
60
55
50
45
40
35
30
1800
1850
1900
1950
2000

Life expectancy in 2012 (Years)

Expected age	Male	Female
At birth	**77**	**83**
If 65 now	**84**	**87**
If 75 now	**88**	**90**
If 85 now	**94**	**95**

Projected increase in Global Population between 2005 – 2020 [illegible]

Why are we living longer?

Better healthcare

Healthy behaviours

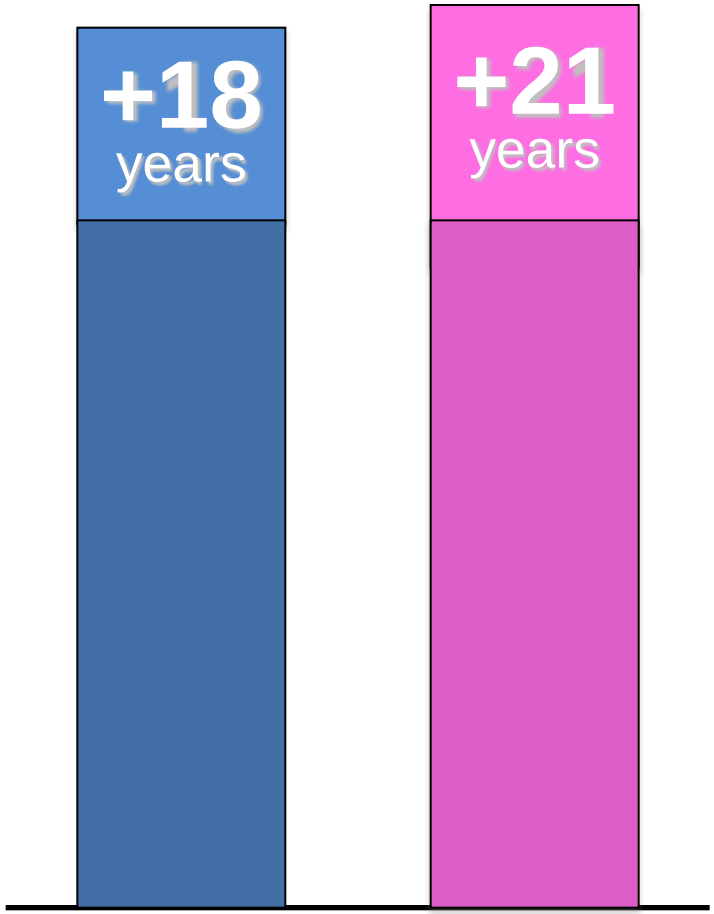
Better environments

More prosperity

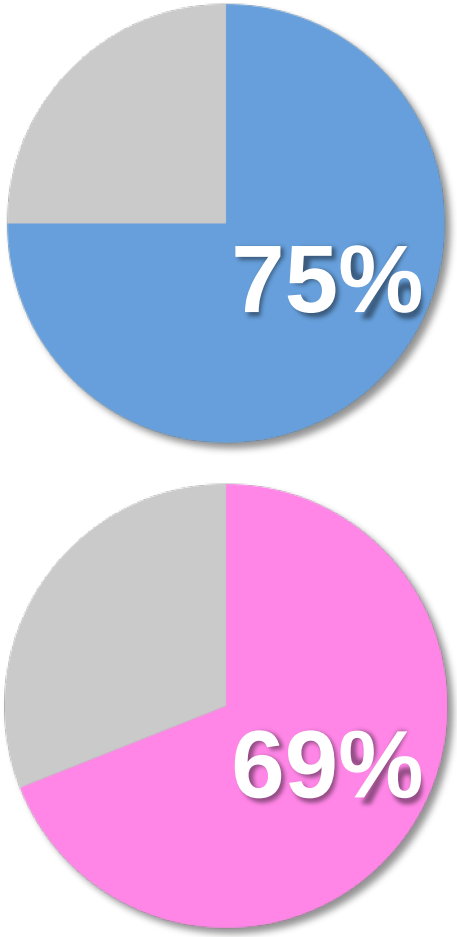
Source: UN Dept of Economic & Social Affairs

Dementia
Stroke
Heart disease
Cancer
Respiratory
Diabetes

Life Expectancy & Healthy Life Years

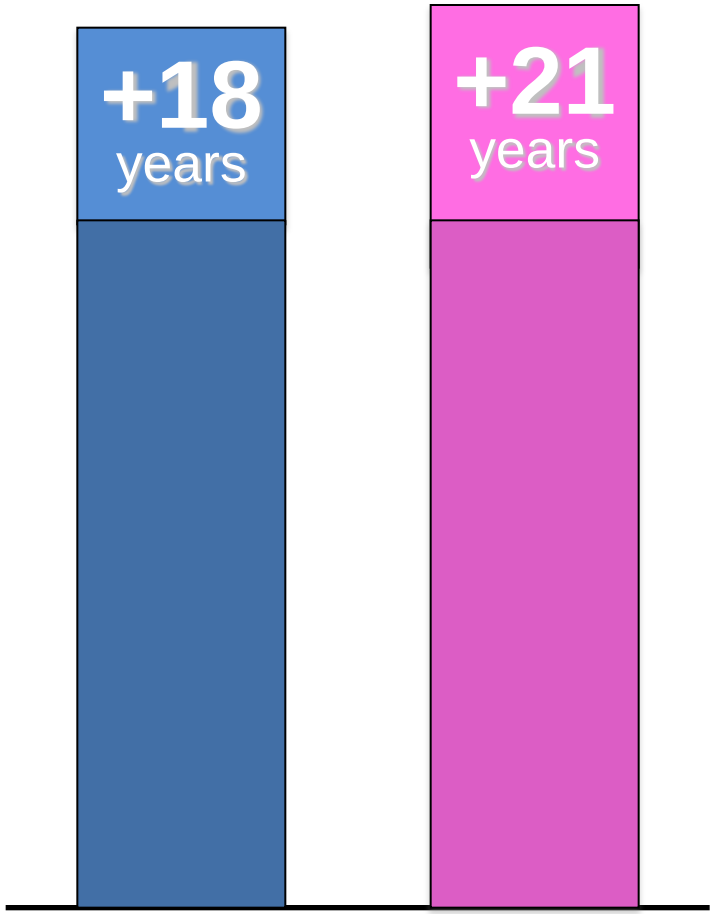


Life expectancy at 65

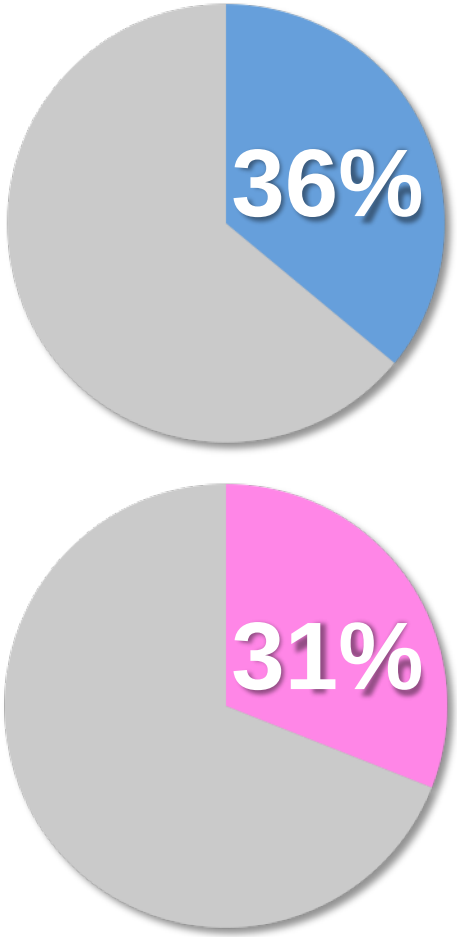


% Healthy Life Years

Life Expectancy & Healthy Life Years



Life expectancy at 65



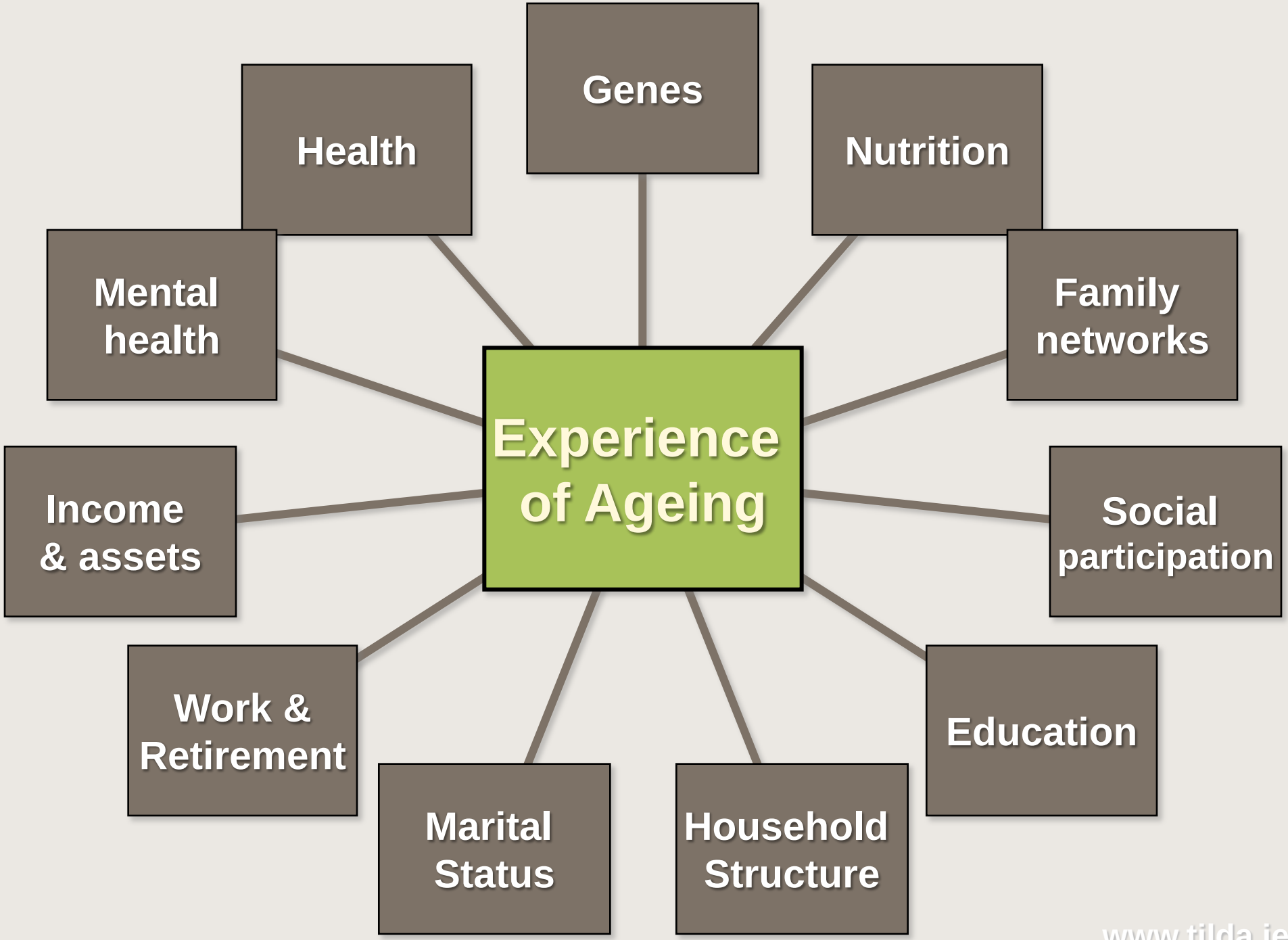
% Healthy Life Years

MORTALITY

- Heart disease
- Stroke
- Cancer
- Respiratory

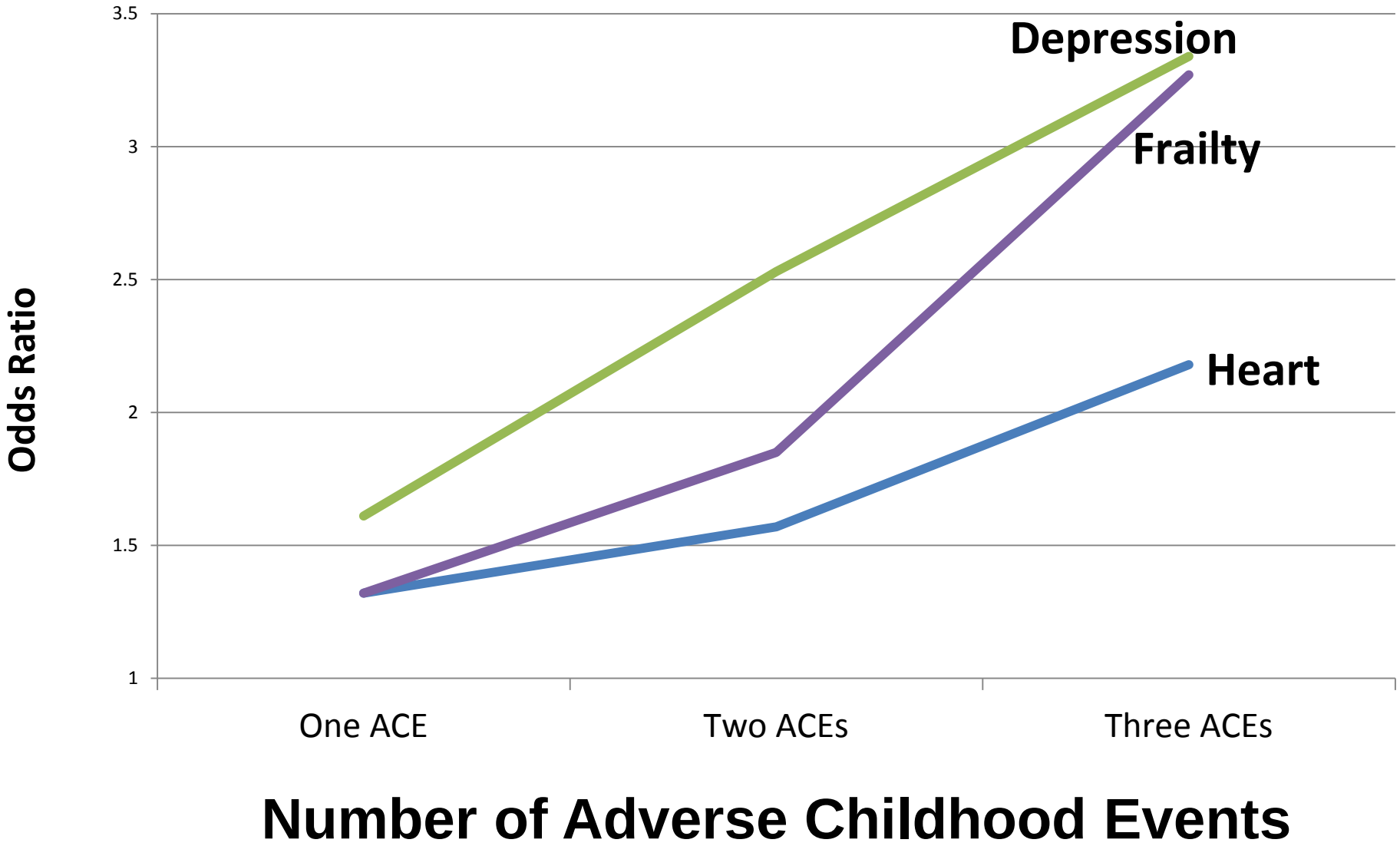
HEALTHY LIFE YEARS

- Dementia
- Falls
- Depression
- Diabetes
- Heart failure
- Arthritis
- Respiratory


Genes
Health
Nutrition
Mental health
Family networks
Experience of Ageing
Income & assets
Social participation
Work & Retirement
Education
Marital Status
Household Structure

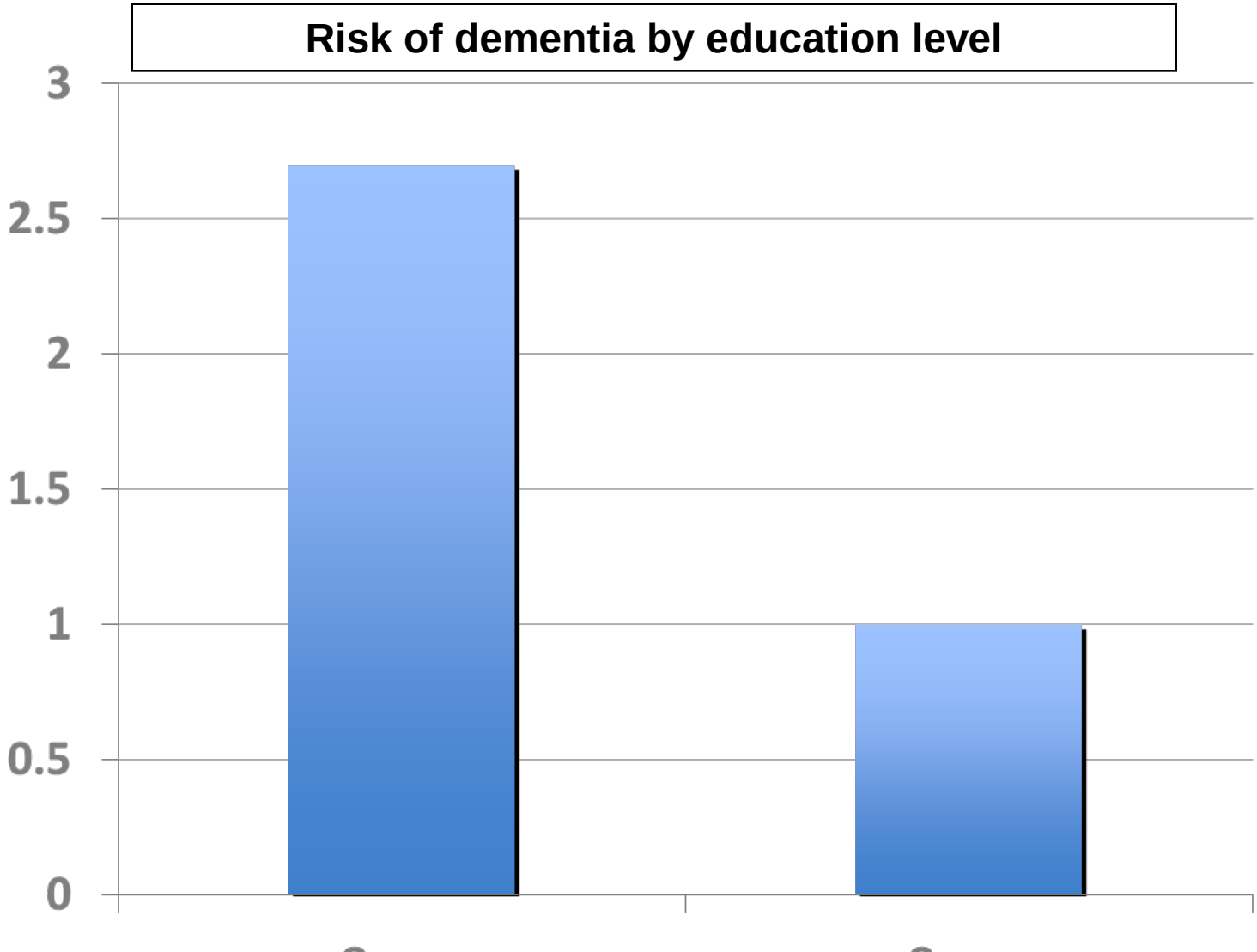
www.tilda.ie

Odds of Disease in Adulthood by the Number of Adverse Childhood Events

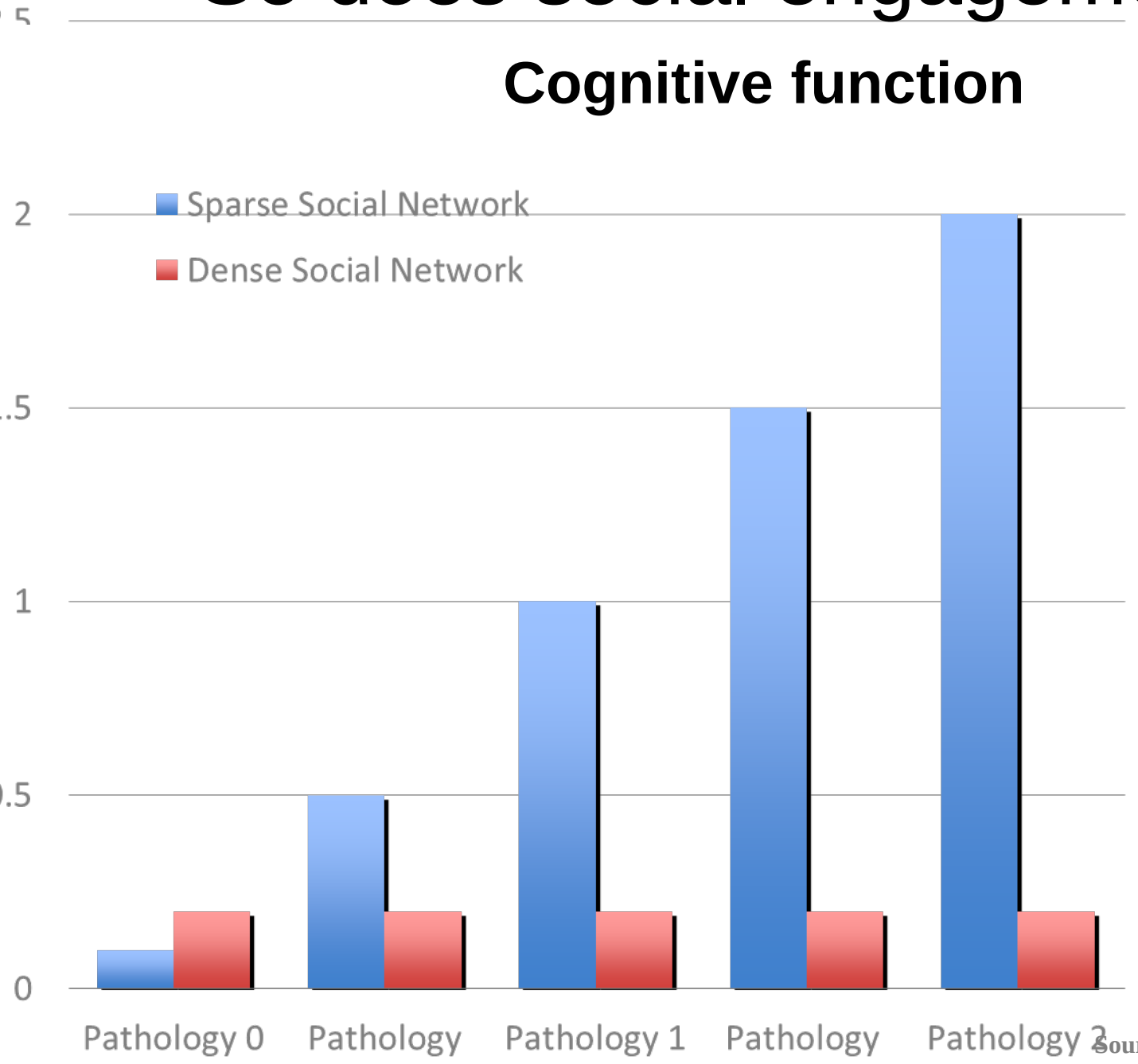


DEMENTIA
One of our greatest fears

Education Protects Against Dementia



So does social engagement…



Source: Bennett et al, Lancet Neurology

Ageing & Social Inclusion

- Quality of life increases with social integration
- Social participation lowers risk:
  - Negative mental health issues
  - Negative physical health outcomes
  - Mortality
- Social isolation, loneliness
  - Predicts a wide variety of negative mental and physical health outcomes
  - Depression
  - Nursing home admission

Functional Consequences

- Increased mortality[1]
- Poor medication adherence[2, 3]
- Unemployment[4,5]
- Functional impairment – cooking, shopping, finances[4]

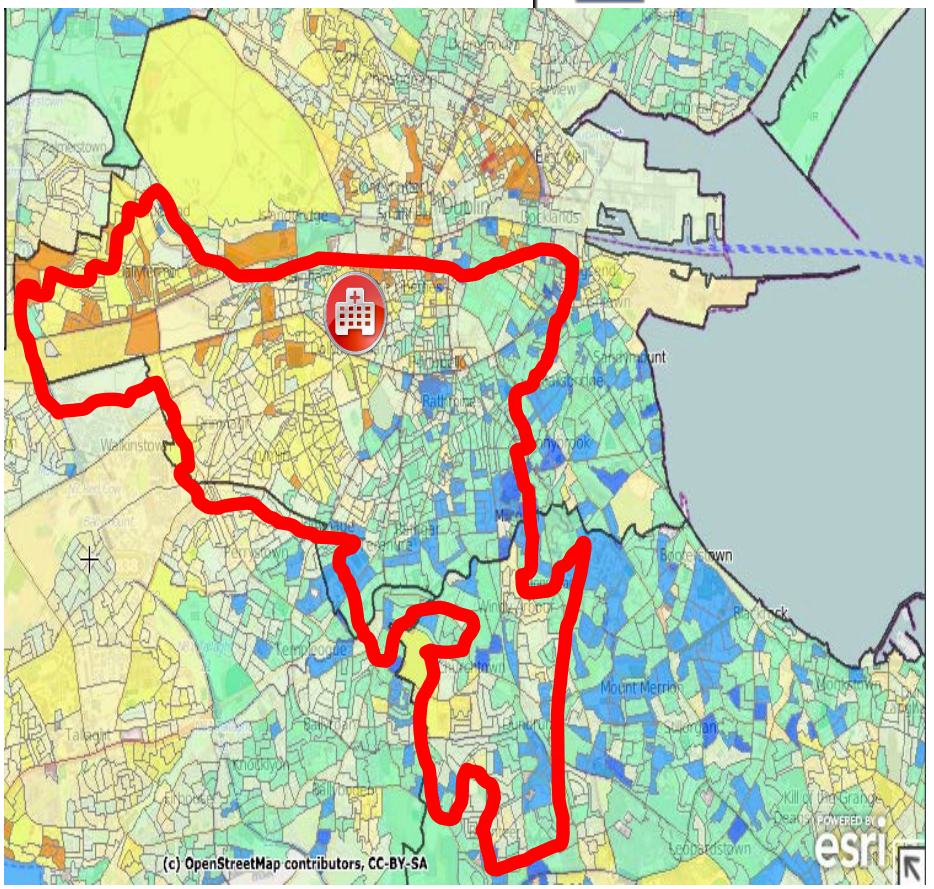
1. Vivithanaporn et al. Neurologic disease burden in treated HIV/AIDS predicts survival: a population-based study. Neurology. 2010;75(13):1150-8.
2. Hinkin CH et al. Medication adherence among HIV+ adults: effects of cognitive dysfunction and regimen complexity. Neurology. 2002;59(12):1944-50.
3. Ettenhofer ML et al. Aging, neurocognition, and medication adherence in HIV infection. Am J Geriatr Psychiatry. 2009;17(4):281-90.
4. Heaton RK et al. The impact of HIV-associated neuropsychological impairment on everyday functioning. J Int Neuropsychol Soc. 2004;10(3):317-31.
5. van Gorp WG et al. Neuropsychiatric predictors of return to work in HIV/AIDS. J Int Neuropsychol Soc. 2007;13(1):80-9.

Successful Ageing

- Exercise
- Smoking
- Moderate alcohol consumption
- Reduced stress
- Healthy diet
- Socialisation
- Reduced stress
- New learning

- Interventions to decrease ageing, fraility, dementia at an earlier time point

www.healthmap.ie



David Robinson, personal communication

HIV and Ageing

- Ageing
  - General trends
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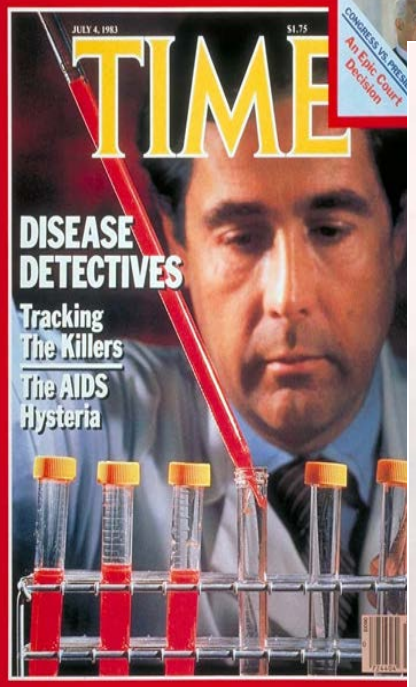
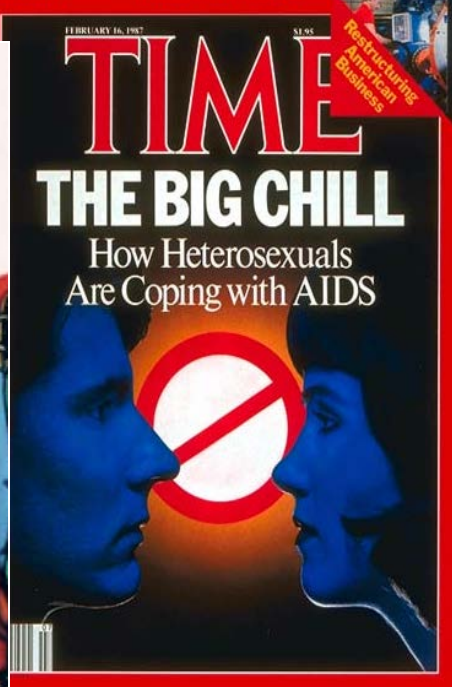
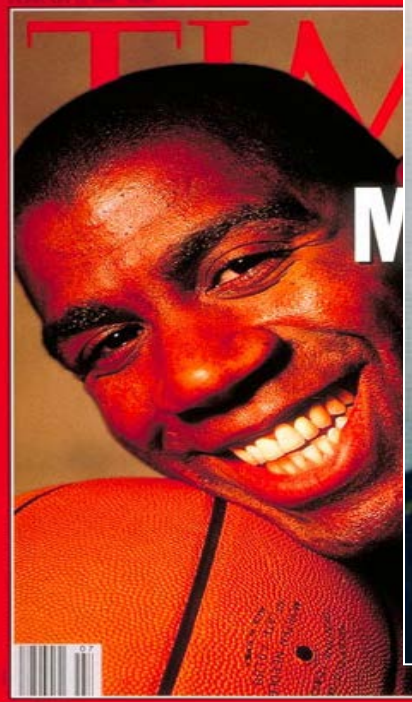
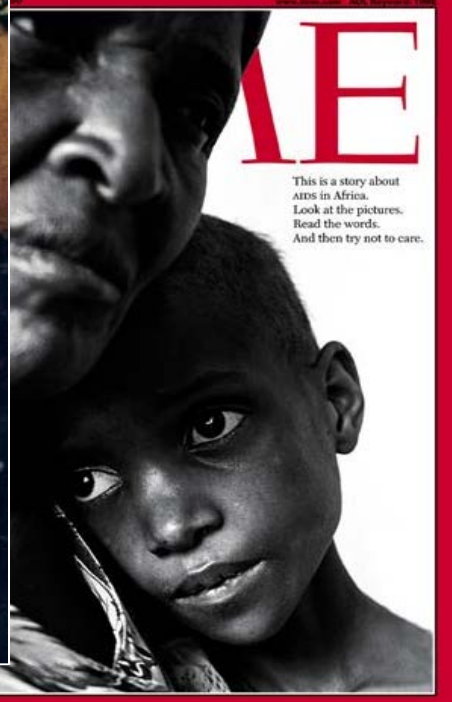

JULY 4, 1983
$1.75
TIME
DISEASE DETECTIVES
Tracking The Killers
The AIDS Hysteria

The Economist
The trap for Turkey
Wall Street's plumbing problem
Lady Gaga, Mother Teresa and profits
Brazil's boiling economy
The farce that is FIFA
JUNE 4TH–10TH 2011
Economist.com
The end of AIDS?
How 5 million lives have been saved, and a plague could now be defeated
€5.80


FEBRUARY 16, 1987
$1.95
TIME
Restructuring American Business
THE BIG CHILL
How Heterosexuals Are Coping with AIDS




This is a story about AIDS in Africa.
Look at the pictures.
Read the words.
And then try not to care.

June 19, 2010 Vol. 24, No. 10
AIDS
Official Journal of the International AIDS Society

Life Expectancy of Recently Diagnosed Asymptomatic HIV-infected Patients Approaches that of Uninfected Individuals

A. van Sighem et al. on behalf of the ATHENA National Observational Cohort Study

- **Life expectancy** for HIV-infected patients (without AIDS) aged 25 yrs at six months postinfection
  - **Men: an additional 52.7 yrs** (versus 53.1 yrs in general population)
  - **Women: an additional 57.8 yrs** (versus 58.1 yrs in general population)

HIV & Age

TIME
IN PARTNERSHIP WITH CNN

Quotes of the Day
"I made a terrible mistake not maliciously, but I made a terrible mistake." – *Richard Armitage*

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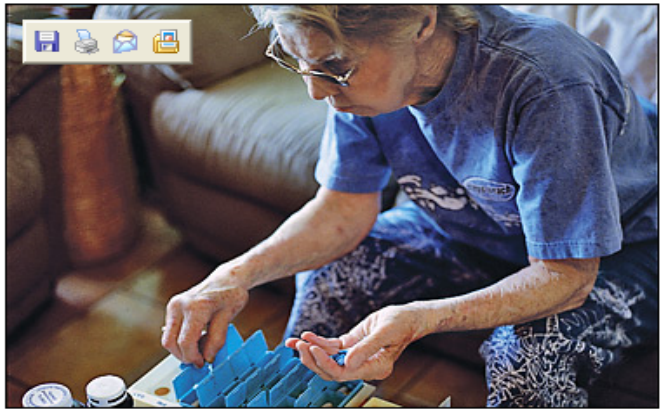


KATJA HEINEMANN / AURORA FOR TIME
Sue Saunders, 73, organizes her daily medication regimen.

From the Magazine | Science

The Graying of AIDS

The growing number of senior Americans living with HIV is facing a generation of doctors and scientists unprepared for their singular problems

By CHRISTINE GORMAN

HOME PAGE | TODAY'S PAPER | VIDEO | MOST POPULAR | Global Edition

The New York Times | International Herald Tribune

GLOBAL EDITION
N.Y. / Region

WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

'People Think It's Over'

Spared Death, Aging People With H.I.V. Struggle to Live

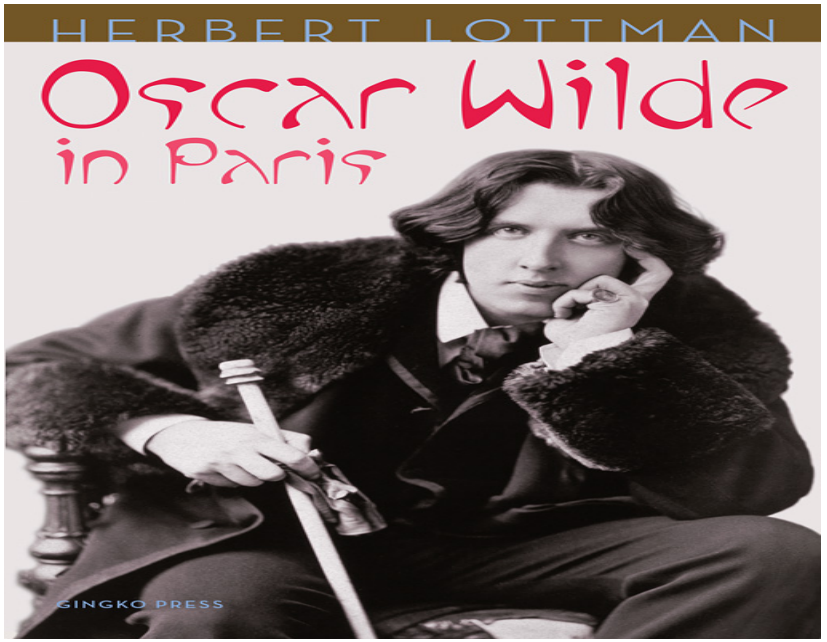
Nicole Bengiveno/The New York Times
In his Midtown apartment, Steve Schalchlin, 59, has a piano that he plays every day. He said his music has kept him alive.

By JOHN LELAND
Published: June 1, 2013

Steve Schalchlin would be the first to tell you he lives in a time of miracles, and about how hard that can be. In 1995, as his body wasted away from AIDS, he took the limited time in front of him as a challenge: he would write songs, make amends, fill his remaining days with life. And by the end, with his digestive system shut down, his figure skeletal, he was ready to die. Then he won a lottery for a new AIDS drug that had been rushed through the approval process.

FACEBOOK
TWITTER
GOOGLE+
SAVE
E-MAIL
SHARE

Ireland – small island in global world



A Differing Era

AIDS patients should be on ordinary wards, says new sex doctor

by **ANNE MARIE HOURIHANE**

AIDS patients in hospital should not be isolated in separate wards, according to Fiona Mulcahy, who has recently been appointed Ireland's first ever consultant specialist in sexually-transmitted diseases.

Mulcahy does not anticipate that AIDS will comprise the majority of her work.

At present, for every ten men who attend the Dublin clinics for other sexually-transmitted disease, just one woman presents herself for treatment. That's just one of the alarming statistics Dr Mulcahy brings to her new job.

'I tell the patients face to face they have Aids . . . and that now is the time to do anything they may have wished to do'

Exclusive: Catherine Troy

The doctor at death's door

Dr. Mulcahy: dealing with a lonely illness.

Irish Times Dec 1st '93

AIDS treatment not available

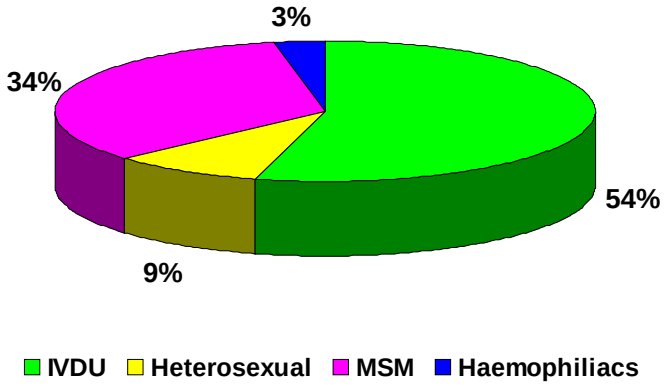
THE IRISH TIMES, Monday, August 30, 1993 C

The President, Mrs Robinson, with former entertainer Mr Anthony McDonnell, a patient at the AIDS unit of St James's Hospital, Dublin. With them are Dr Fiona Mulcahy (left) and Sister Nora Magee. Photograph: Jack McManus

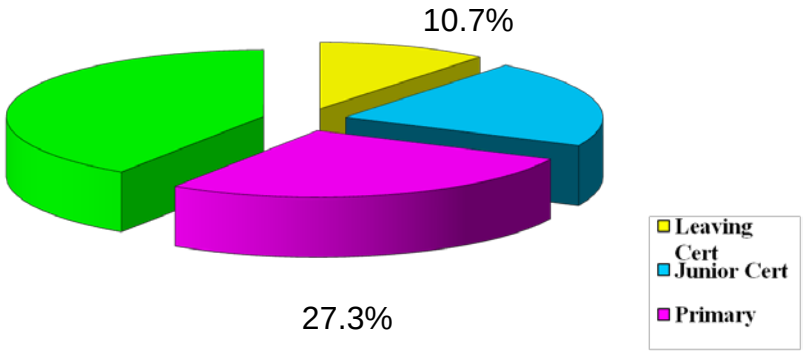
President visits AIDS patients

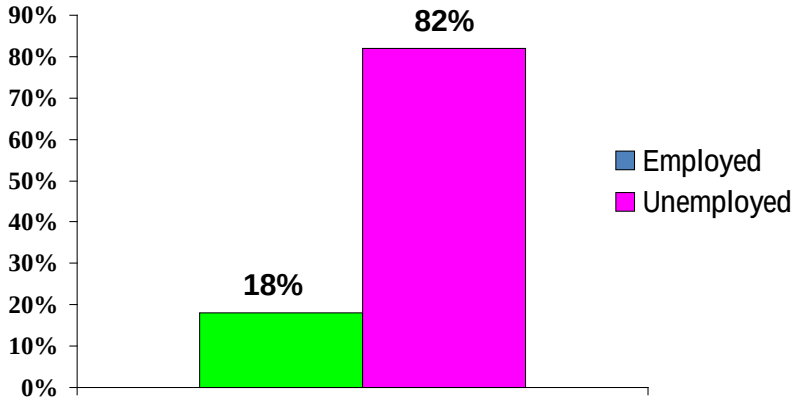
HIV in 1999

800 patients



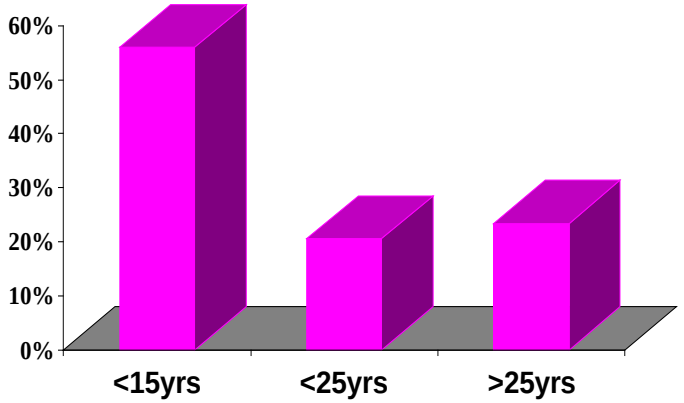
Educational History





Employment Status

Age at First Incarceration: n=130



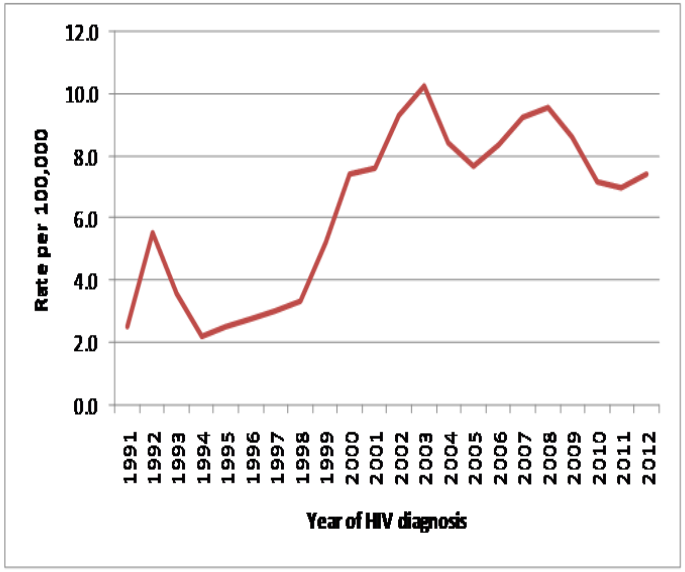
Clarke et al, HIV Med.2003:1;33-37

Celtic Tiger

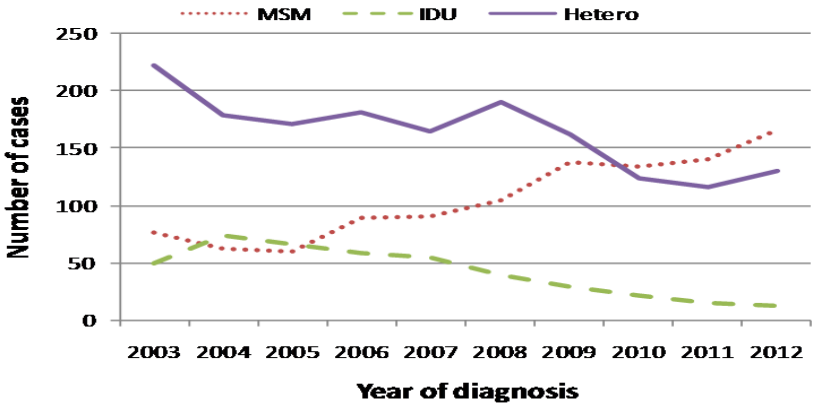
- Sexual health
- Migration
- Successful treatments

HIV in Ireland in 2013
- **A Chronic Disease**

Health Protection Surveillance Centre
Lárionad Faire um Chosaint Sláinte



Trends in new HIV diagnoses (per 100,000 population), 1991 to 2012



Trends in new HIV diagnoses by probable route of transmission 2003 to 2012

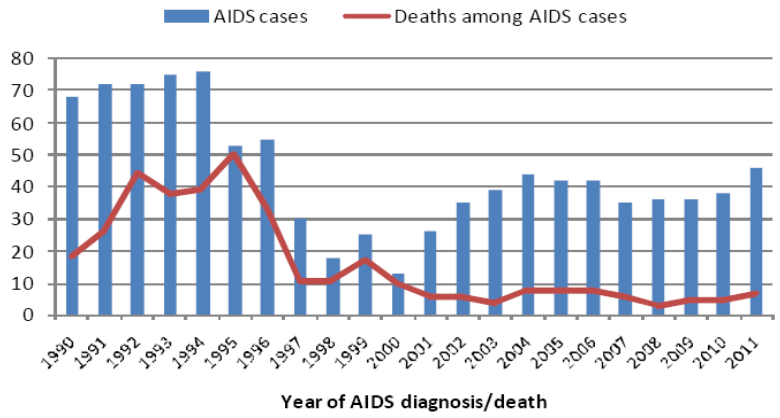


Figure 6.1: AIDS cases and deaths among AIDS cases, 1990 to 2011

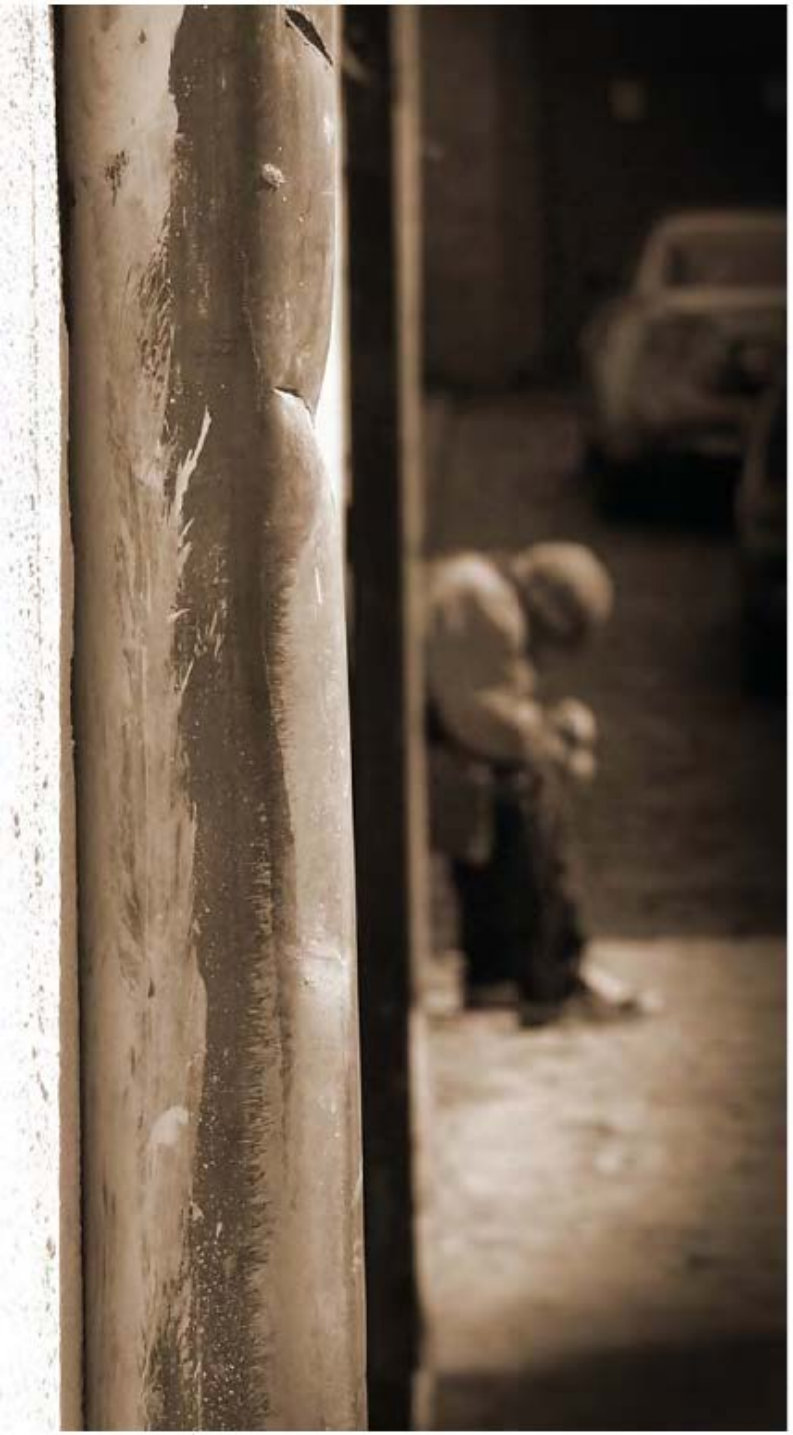
- 341 newly diagnosed……BUT

  - Highest number of new cases in MSMs (48.7%)
    - 38% heterosexual; 4% IDUs (4%)
  - 48% presented late (CD4<350) with 24% having CD4<200
  - 33 reported AIDS events occurred in newly diagnosed patients
  - 9% >50yrs old

Non-Engaged – Disparity of Outcome

- IDUs
  - 25% history of IDU
  - 148 had a CD4 count <350 x 10^6/L and not on HAART
  - 1768 number of missed clinic appointments between January 2006 & June 2008
    - 1549 (87%) in IVDUs
  - 187 HIV positive patients had two or more hospital admissions
    - 145 (77%) of these were in individuals with a history of IVDU

Personal communication: Dr Saloni Surah



Injection Drug Users

Recent screening in drug treatment centres in Dublin:

>50% reported never having had a HCV/HIV test

Of those tested, 50-80% infected with HCV

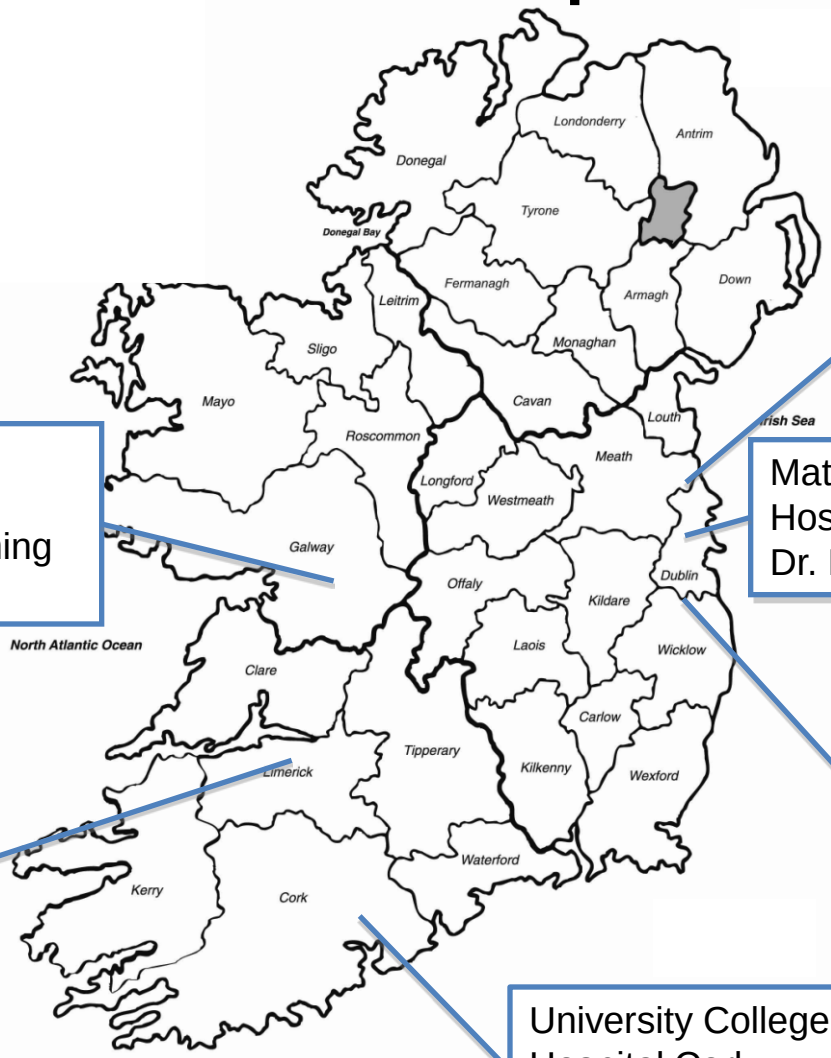
<20% have been treated for HCV

Risk of cirrhosis >20%

Use of acute hospital services: 8 x higher

Life expectancy: 30 years shorter

Current HIV Service Delivery – Public Hospitals



Beaumont Hospital
Prof.Samuel Mc Conkey;
N=359

Mater Hospital
Dr. Patrick Mallon; **n=~700**

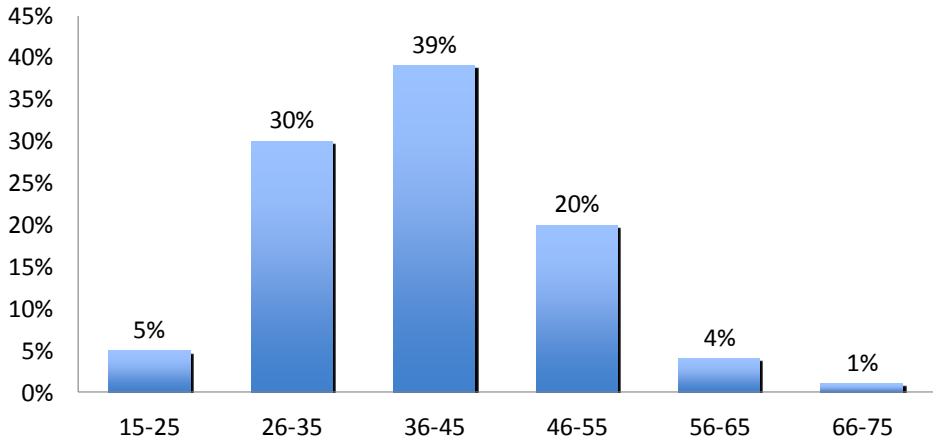
St. James's Hospital
Prof. Colm Bergin
Prof. Fiona Mulcahy
N= 2150

University College Hospital Cork
Prof. Mary Horgan; **n=365**

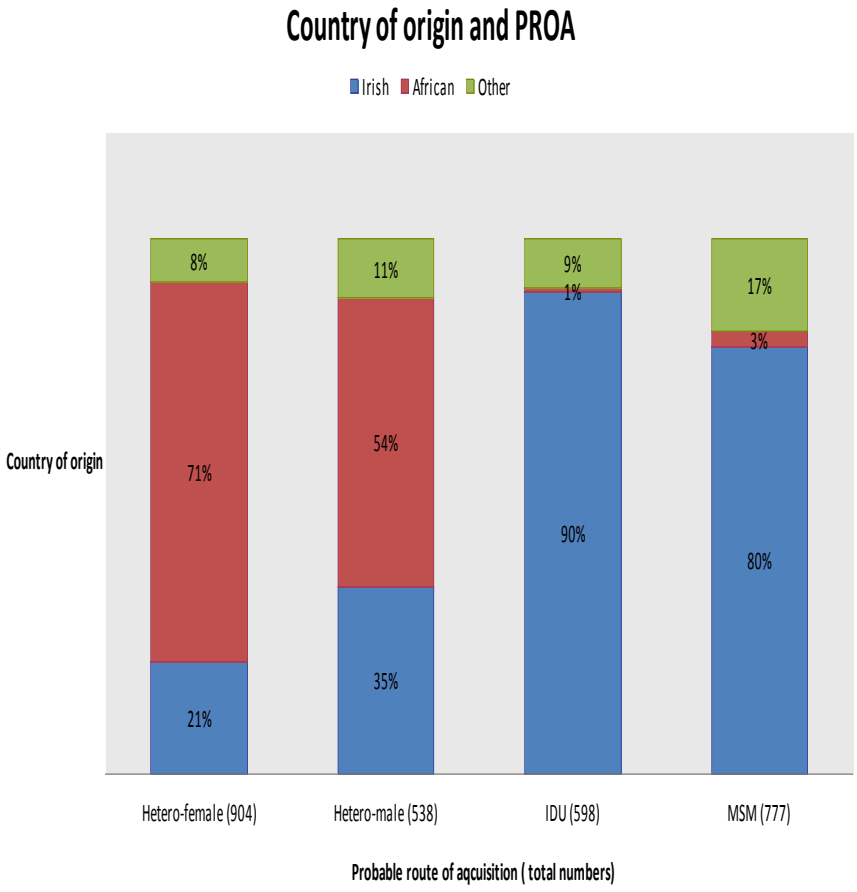
Limerick Regional Hospital
Dr. Busi Mooka
N=77

University College Hospital Galway
Dr. Catherine Fleming
N=170

Patients Accessing Ambulatory Care for HIV-infection in Ireland (PACHI-1)

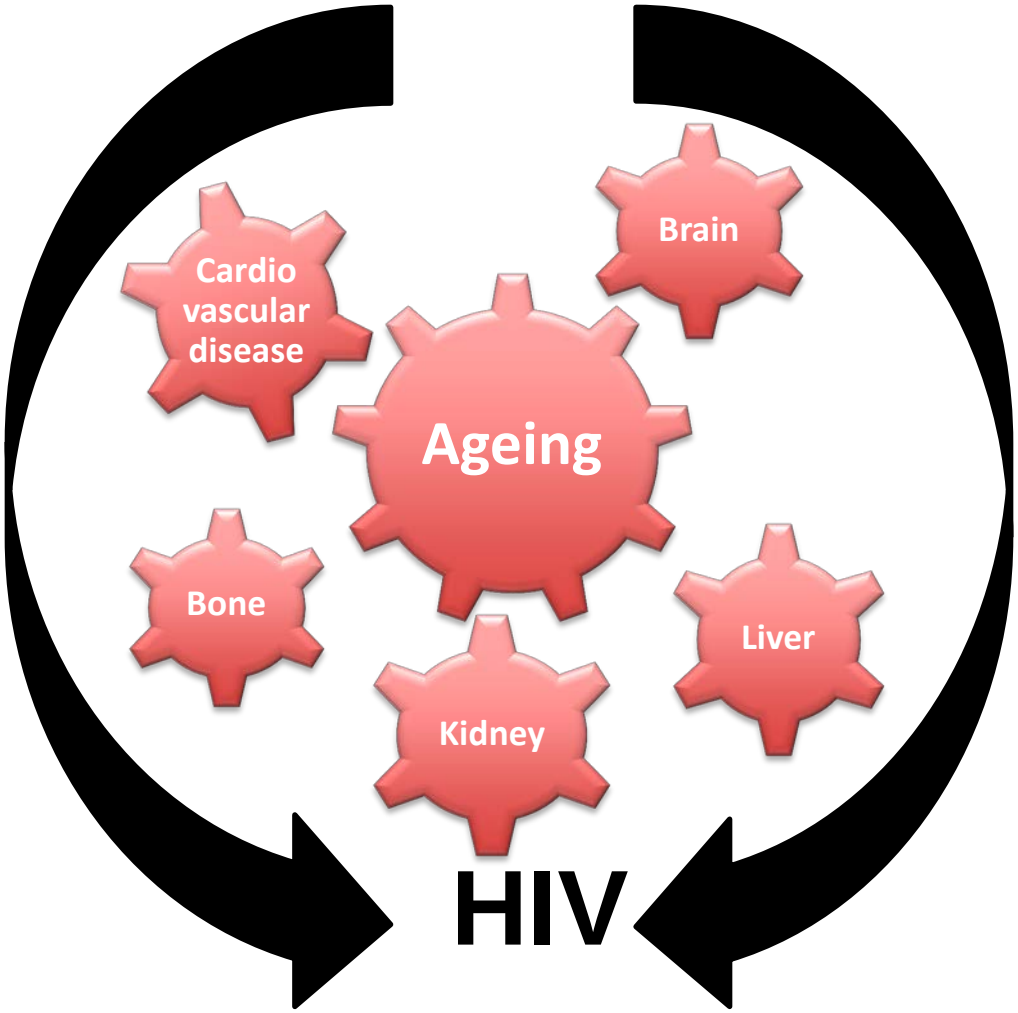


25% >45yrs



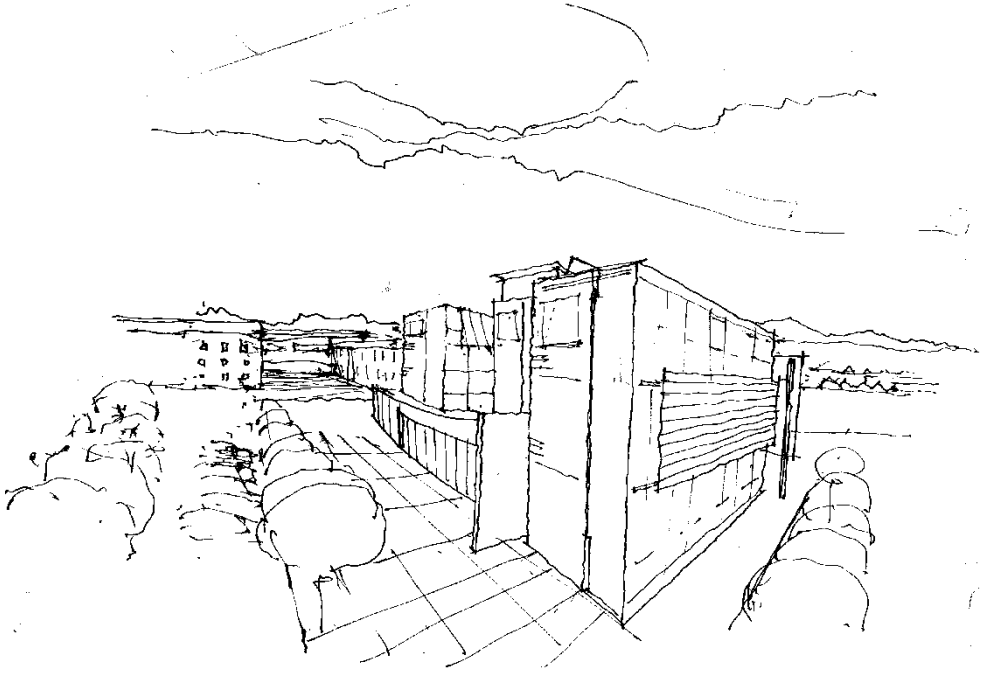
HIV Research

- Clinician-delivered, multidisciplinary
  - HIV Molecular Research Group (HMRG)
  - HIV Clinical Therapeutic Trials
  - HIV and Cardiovascular Disease
  - HIV and Vaccine Work
  - HIV Epidemiology (Clinical and Molecular)
  - HIV and Bone Health
  - HIV and Renal Disease
  - HIV Oncology
  - HIV and Liver Disease
  - HIV and Syphilis
  - HIV and Pregnancy
  - **HIV and Cognitive Function**



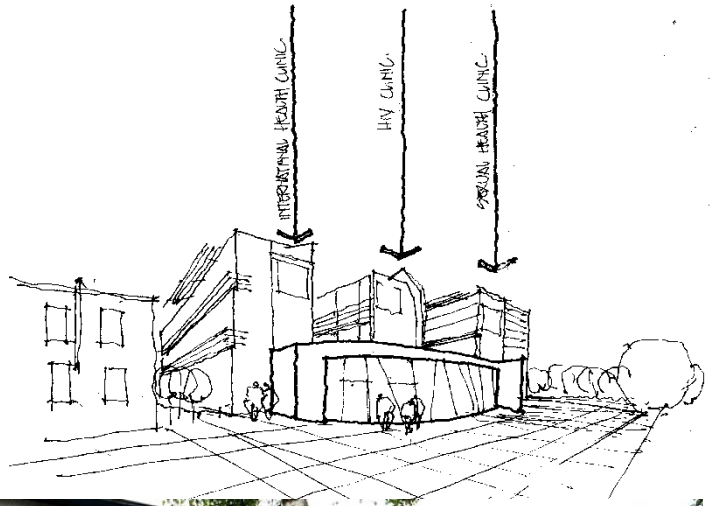
TREATMENT WITH DIGINITY

THE
GUIDE
CLINIC
ST JAMES'S HOSPITAL

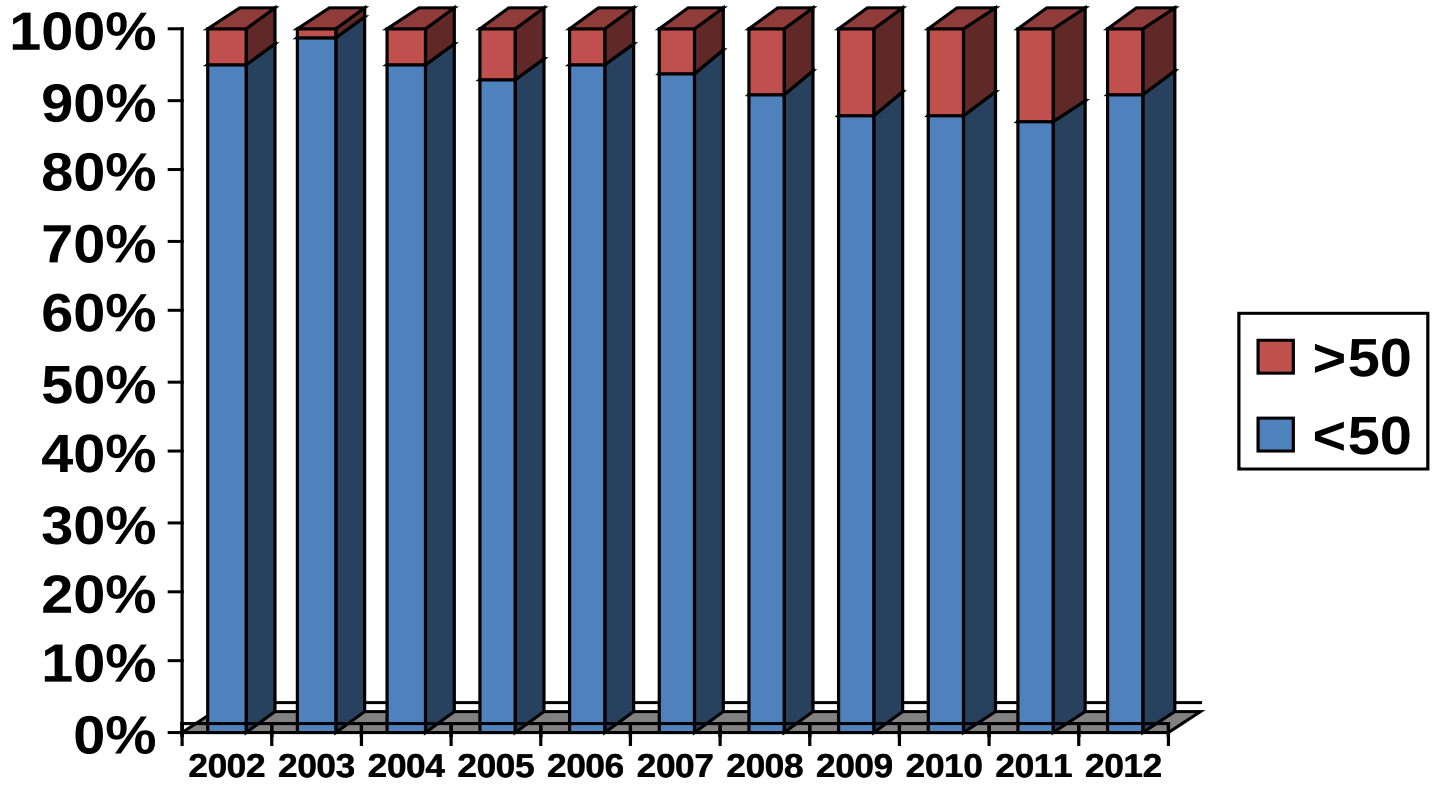


SKETCH PERSPECTIVE SHOWING NEW HOSPITAL FIVE IN CONTEXT OF NEIGHBOURING UNITS. NEW DEVELOPMENT MUST ADDRESS AND DEFINE NEW PUBLIC SQUARE

As one of the main problems with the existing building is the lack of identity and absence of an entrance condition the new structure should establish a strong front entrance to act as a landmark



% new HIV diagnoses >50yrs: 2002-2010

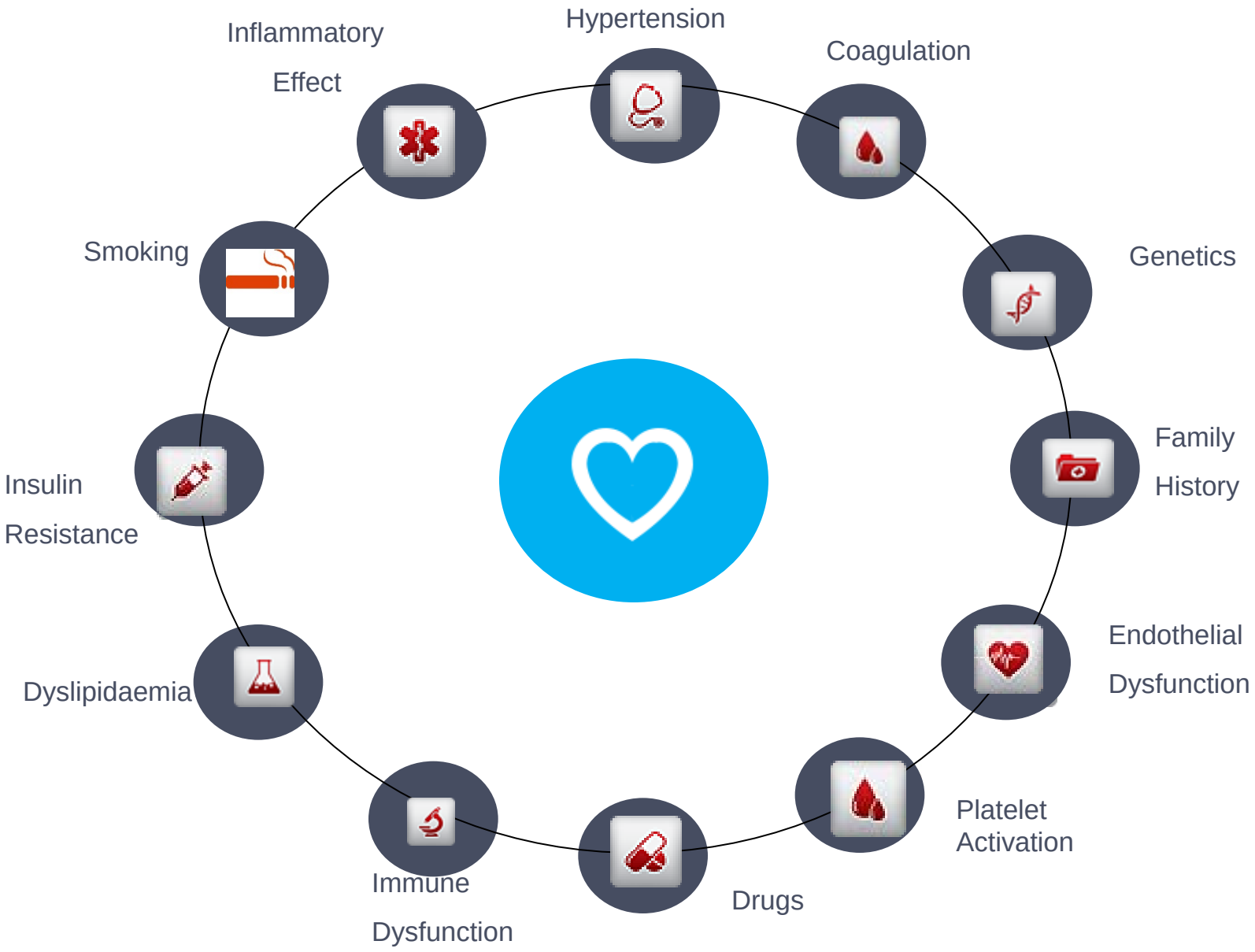


18% of patients attending THE GUIDE CLINIC ST JAMES'S HOSPITAL are >50 years

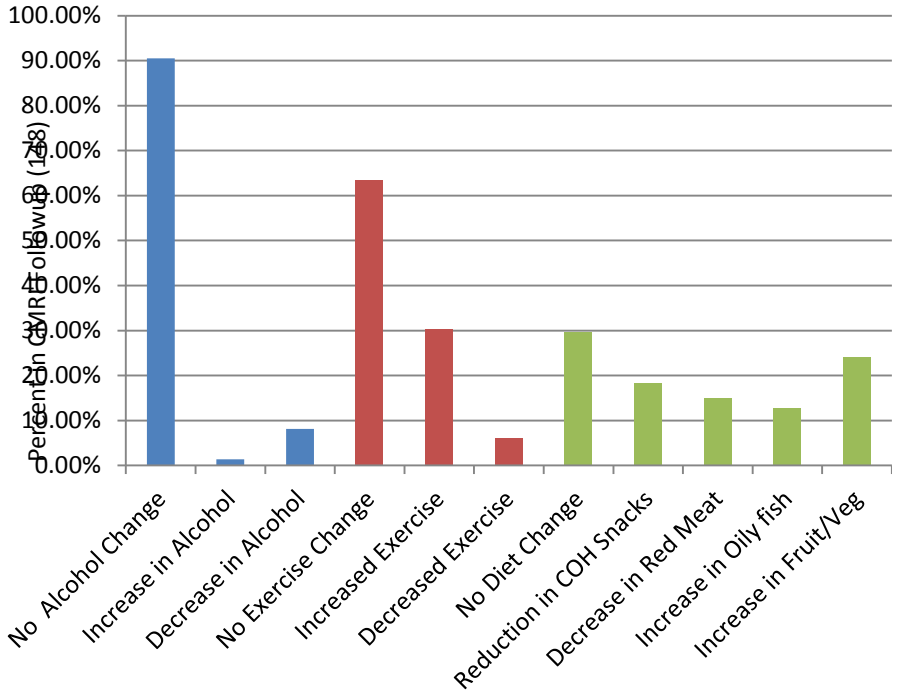
THE GUIDE CLINIC
ST JAMES'S HOSPITAL

Cardiac Dysfunction in HIV+ Men

Causes of CVD in HIV



Interventions And Behaviour Modifications Following A Cardiovascular MRI In HIV-Infected Patients



- 8% decreased weekly alcohol intake
- 30% increased exercise
- 18% reduced COH snacks
- 15% decreased red meat
- 13% increased oily fish
- 24% increased fruit/veg intake
- 13% of patients self reported weight loss

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HIV-Age Clinic

- Pilot study of patients ≥ 55 y.o.
- 147 patients in this age group
- 36 patients assessed to date (28 males, 8 females)
- Avg age: 58.5 (range 55-74)

- Issues addressed:
  - Retroviral disease
  - Co-morbidities
  - Smoking/Alcohol/Drug use
  - Medications
  - Vaccinations
  - Cardiovascular risk
  - Bone health
  - Neurocognitive issues
  - Sexual health
  - Psychological health

HIV-Age Clinic - Co-morbidities

Co-morbidity	%	n
Dyslipidaemia	33	12
Diabetes	19	7
Hepatitis C	17	6
Hypertension	17	6
Renal impairment	17	6
IHD	11	4
Lymphoma	8	3

J. Woo (unpublished data)

HIV-Age Clinic

- Smoking –
  - Current smokers: 33% (12)
  - Ex-smokers: 6% (2)
  - Non-smokers: 61% (22)
- Medications:
  - All on ARVs
  - Avg number non-ARV meds **3.5** (SD 2.7, range 0-10)
  - Avg number total meds **5.7** (SD 3.0, 1-13)

J. Woo (unpublished data)

HIV-Age Clinic

- Bone Health
  - Number of patients having DXA scan – **36%**
    - Osteopaenia: **62%**
    - Osteoporosis: **15%**
    - Vertebral fracture: none

J. Woo (unpublished data)

Burden of disease

Men with osteoporosis	5,490,510	37,127
Women with osteoporosis	22,029,280	129,309
Prevalence in male population aged >50 years	6.6%	6.2%
Prevalence in female population aged >50 years	22.1	20%
Prevalence in total population	5.5%	3.7%
Hip fracture incidence women (/100,000/yr)	-	406
Hip fracture incidence men (/100,000/yr)	-	191
New fractures (rate/1,000)	19.0	14.5
Cost of incident fractures	24, 574 (€m)	125 (€m)
Long-term disability	10,718 (€m)	62 (€m)
QALYs lost	57,243 (€m)	426 (€m)
Cost of osteoporotic fractures (per capita)	€2,528	€3,399

Very high risk

3. Kanis et al Arch Osteoporos 2013 8:144

Who to screen with DXA

	EACS 2013[1]	CID 2010[2]
HIV as 2º cause	Consider	Yes
Post-menopausal women	Yes	Yes
Men > 50 yrs	Yes	Yes
Repeat risk assessment	2 years	2-5 years
Steroid exposure	Yes	Screen
Hypogonadism	Yes	Screen
FRAX	All >40 yrs	T>-2.5 and ≤-1
Fragility fracture	Yes	Yes

- Repeat DXA after 3-5 5 years in these groups
- Loss and gain in BMD in those switching to and from TDF or PI regimen – clinical significance undetermined

1. EACS Prevention and Management of Non-Infectious Co-Morbidities in HIV 2013
2. 2. McComsey GA et al. CID 2010;51:937-46

HIV-Age Clinic

- Psychological health
  - Hx of depression: 31% (11)
  - Self-reporting of persistent low mood: 28% (10)

J. Woo (unpublished data)

The Case for Cognitive Screening in HIV Clinics

P McNamara, J Redmond, C Bergin, C Doherty
Department of Neurology, Hospital 5 HCC, St. James's Hospital, Dublin 8

Abstract
A retrospective chart review was carried out at the HIV clinic in St. James's Hospital, Dublin to examine the impairment through the use of surrogate markers for cognitive impairment. 500 consecutive hospital charts were 306 men and 194 women. Median age was 37. The most common mode of transmission was heterose CD4 < 200. 78.6% were on antiretroviral therapy and 72.26% were virally suppressed. 69/500 patients (13 positive surrogate markers for cognitive impairment. The surrogate markers used were subjective complaint psychiatric diagnosis post diagnosis with HIV, neurological complications and radiological evidence of atrop using logistic regression showed significant relationships only with gender and year of diagnosis. This figure international prevalence rates of cognitive impairment and demonstrates that surrogate markers are no mat cognitive screening. We have since commenced structured prospective screening to obtain a true prevalenc in this population.

Neuro-cognitive Studies

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- Prevalence study (**604 pts**)
  - Screening for Cognitive impairment using BNCS
- Detailed Neuropsychological Study (**104 pts**)
  - To examine pattern of neuropsychological impairment
- 3T MRI (**50 pts**)
  - VBM (to assess focal grey matter atrophy)
  - DTI (to assess white matter tract integrity)
  - Resting state fMRI (to assess default mode network abnormalities)
  - Routine clinical scans (T1, T2, FLAIR)
- CSF (**13 pts**)
  - Flow cytometry of matched CSF and blood

P McNamara, PhD thesis

Prevalence Study

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- **604 patients**
  - 78.8% male,
  - 70.9% Irish, 16.5% African, 8.6% European, 4% other
  - Mean age 40.9 (18 – 77)

- **MOT**
  - Heterosexual 198/604 (32.8%)
  - MSM 298/604 (49.3%)
  - IVDU 93/604 (15.4%)
  - Other 15/604 (2.5%)

- **504/604 (83.4%) on HAART, 88.7% virally suppressed**

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Positive screen for Cognitive Impairment

51.5%

Patricia McNamara

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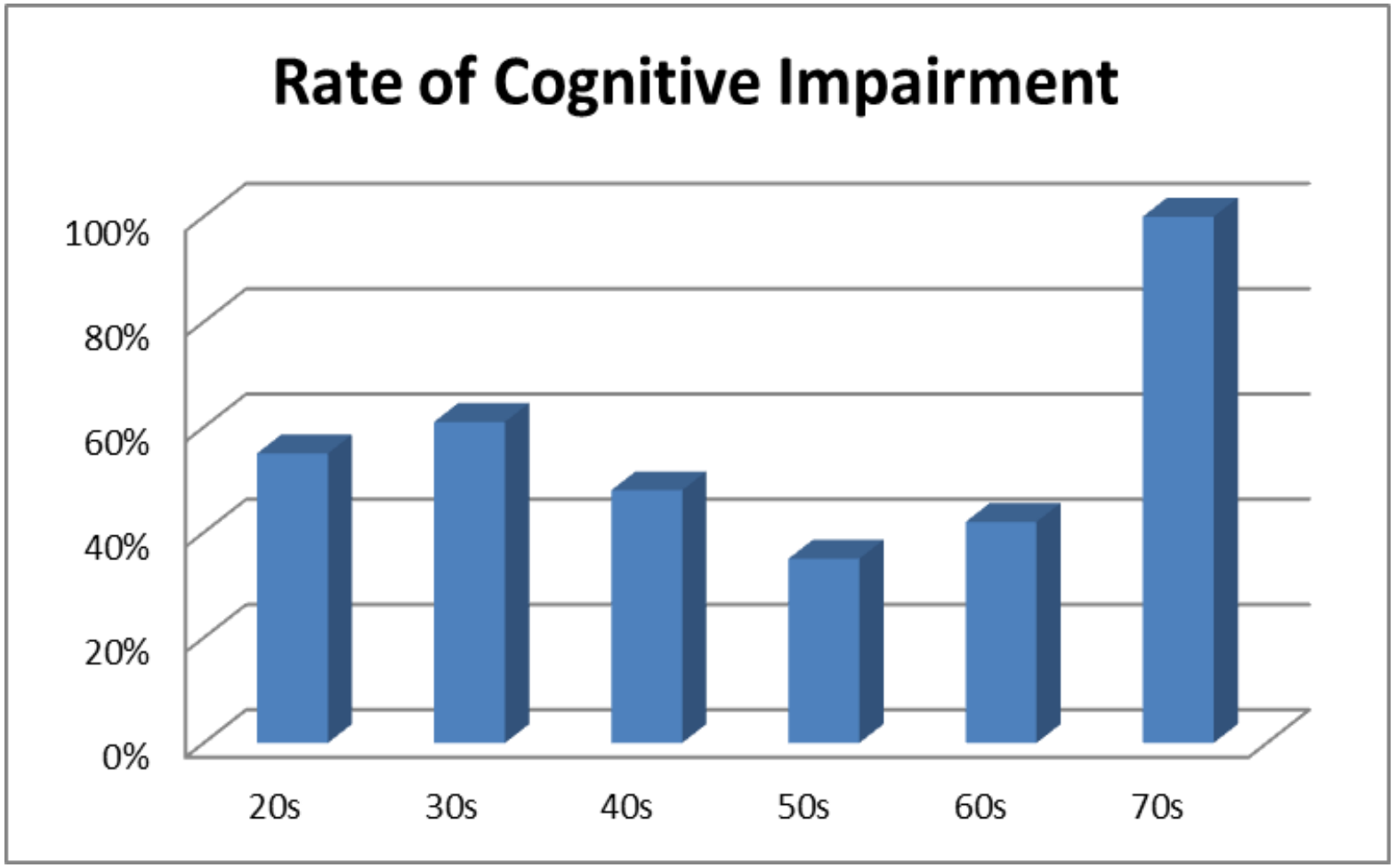
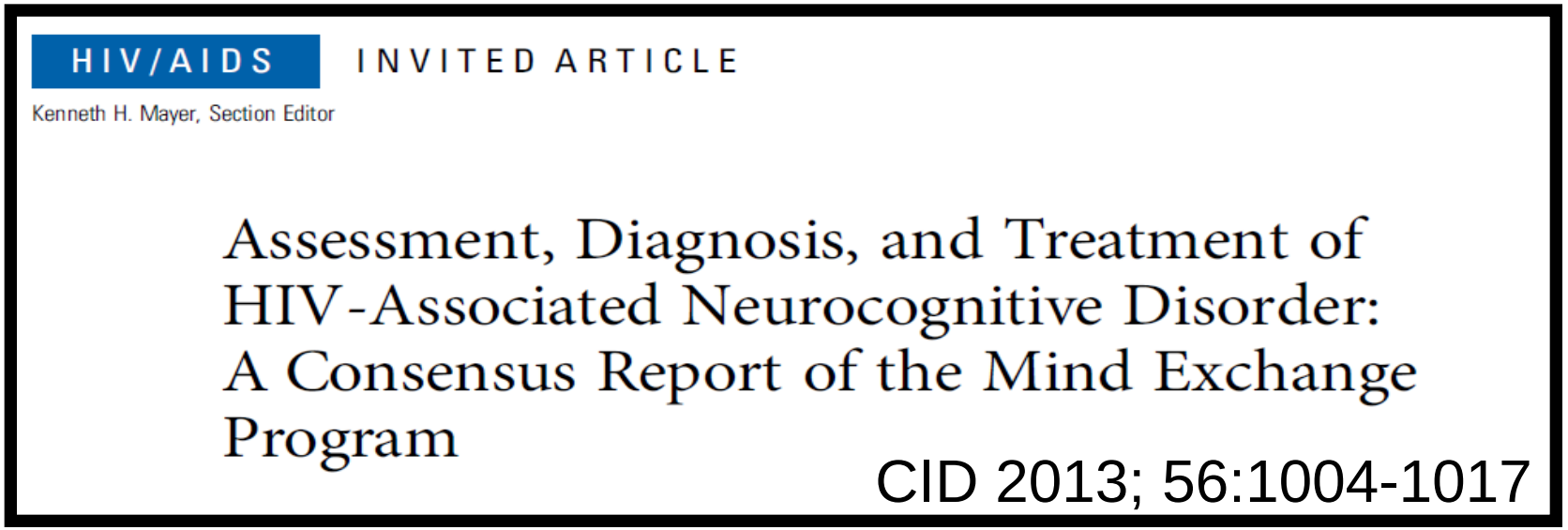


P McNamara, Personal Communication

Conclusions

- 51.8% had a positive screen.
- Potential risk factors identified.
- Effect of mood and mood disturbance may represent part of the spectrum of HAND
- Screening and identifying patients with cognitive impairment is important and necessary


HIV/AIDS INVITED ARTICLE

Kenneth H. Mayer, Section Editor

Assessment, Diagnosis, and Treatment of HIV-Associated Neurocognitive Disorder: A Consensus Report of the Mind Exchange Program

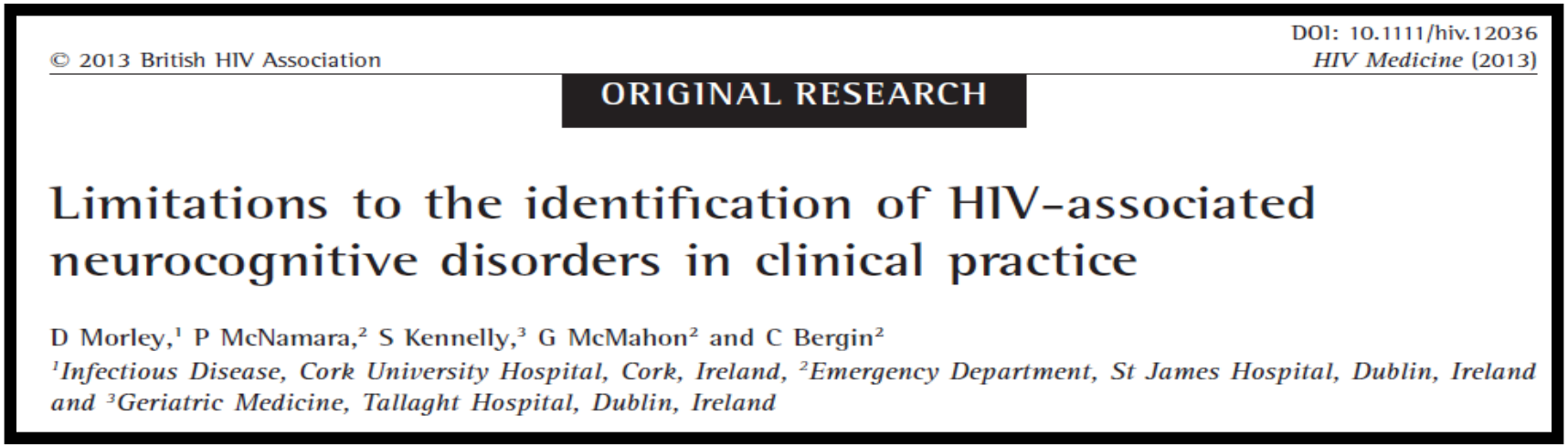
CID 2013; 56:1004-1017

Conclusions

- 50% had a positive screen for CI
- 60% of a subset met criteria for HAND
- Demonstrated cortical and degenerative features
- Evidence of grey matter atrophy
- Evidence of loss of white matter integrity

Future Directions

- Longitudinal follow up is required
  1. Neurodegenerative ?
  2. Progressive ?
  3. Do patients with abnormalities in only one domain represent an earlier form of the same condition ?



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DOI: 10.1111/hiv.12036
HIV Medicine (2013)

ORIGINAL RESEARCH

Limitations to the identification of HIV-associated neurocognitive disorders in clinical practice

D Morley,[1] P McNamara,[2] S Kennelly,[3] G McMahon[2] and C Bergin[2]
[1]Infectious Disease, Cork University Hospital, Cork, Ireland, [2]Emergency Department, St James Hospital, Dublin, Ireland and [3]Geriatric Medicine, Tallaght Hospital, Dublin, Ireland

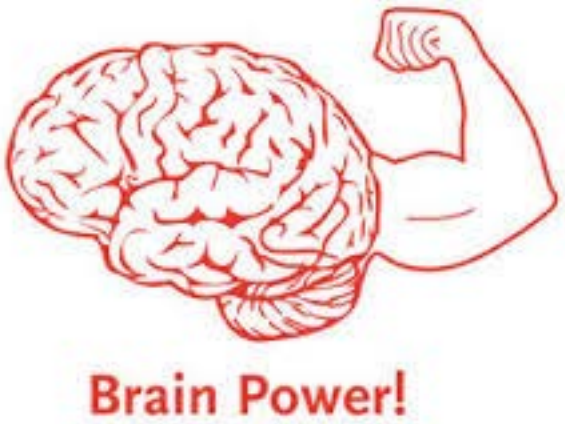
HIV and Ageing

- Ageing
  - General trends
- HIV-related
  - Disease-related prognosis
  - Disease-related and risk-related factors
- Interventions
  - Nutritional
  - Cardiovascular risk interventions
  - **Exercise**
  - “Socialisation”

Non-pharmaceutical interventions for people living with HIV:

Aerobic Exercise

“True enjoyment comes from activity of the mind and exercise of the body; the two are ever united” – Wilhelm von Humboldt



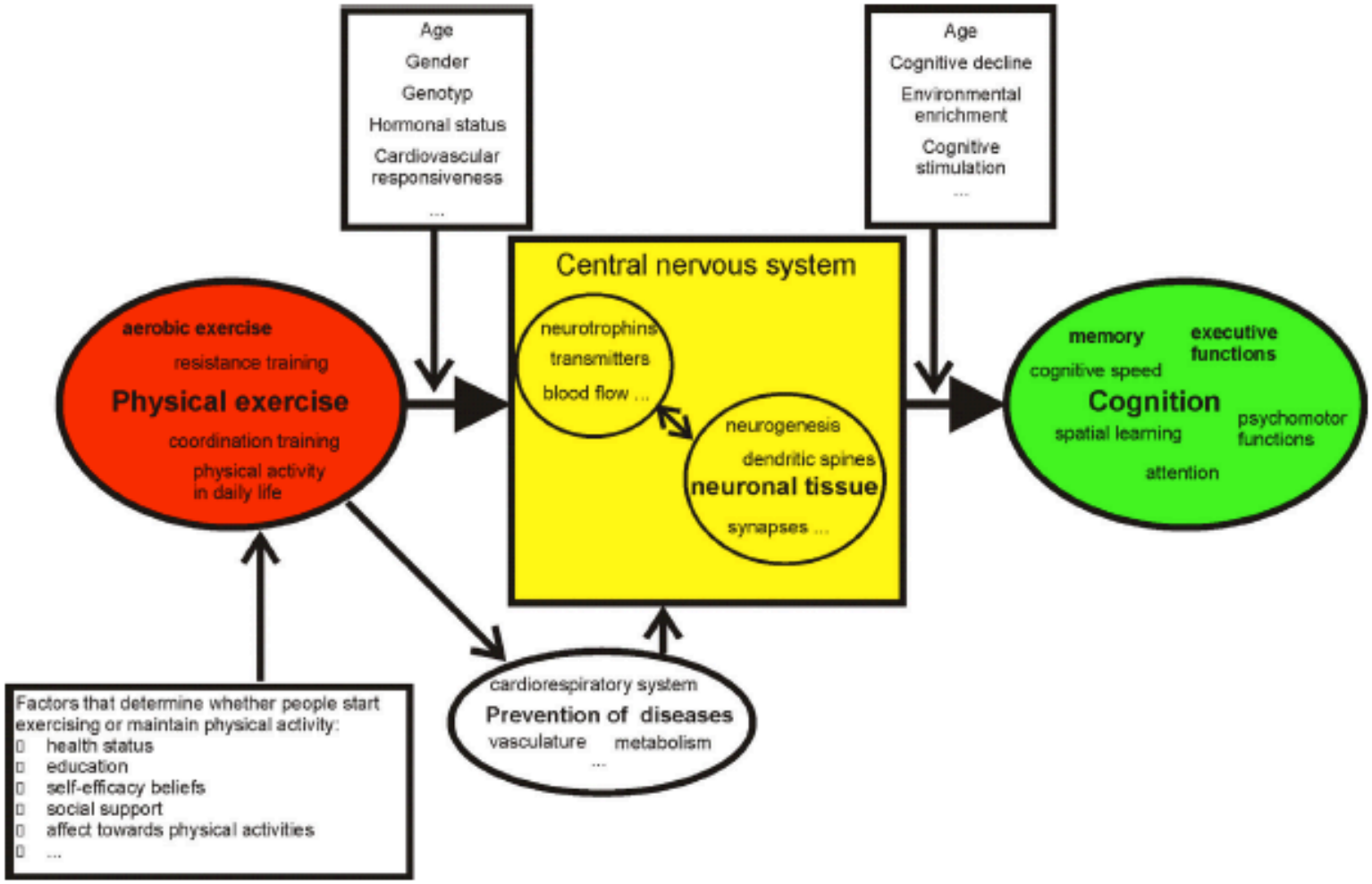
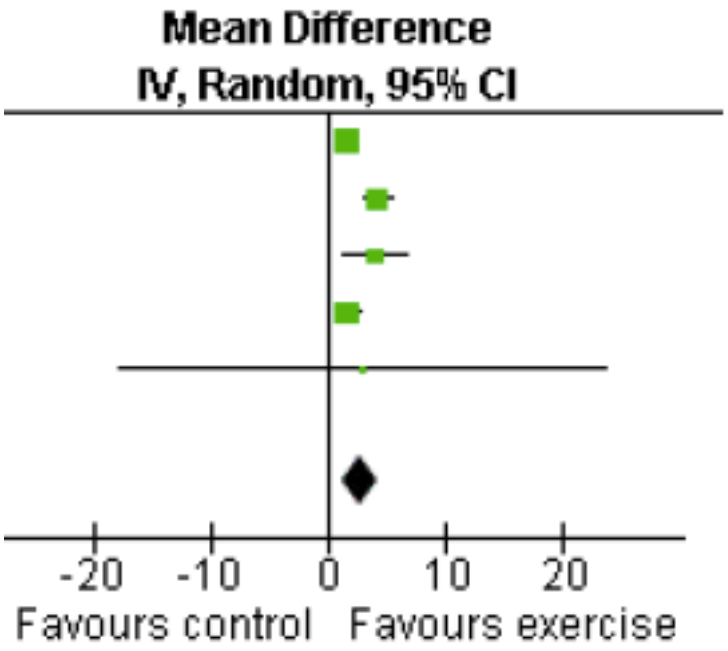


Fig. 3. Summary of the possible relationship between physical exercise, neuroplasticity and cognition with possible moderator variables which might influence exercise behavior, the impact of exercising on the central nervous system and whether changes in the nervous system translate into measurable changes in cognitive variable. This schematic summary is far from being complete and neglects possible reciprocal connections between the variables which have rarely been studied so far.

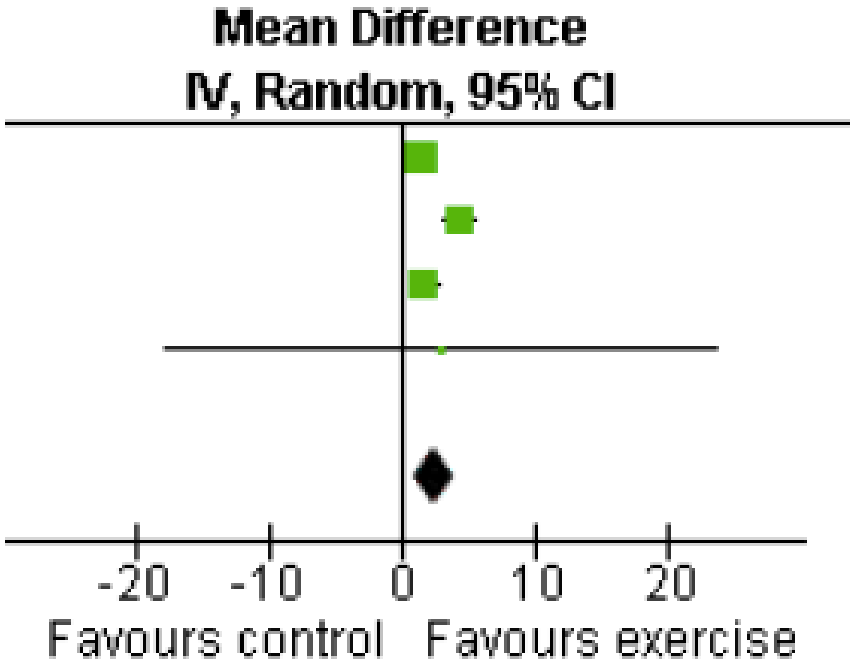
Hotting et al., Neuroscience and biobehavioural reviews. 2013

Clinically important improvements in fitness (VO2max) with regular exercise

Constant or interval aerobic exercise compared with no exercise. Outcome VO2max



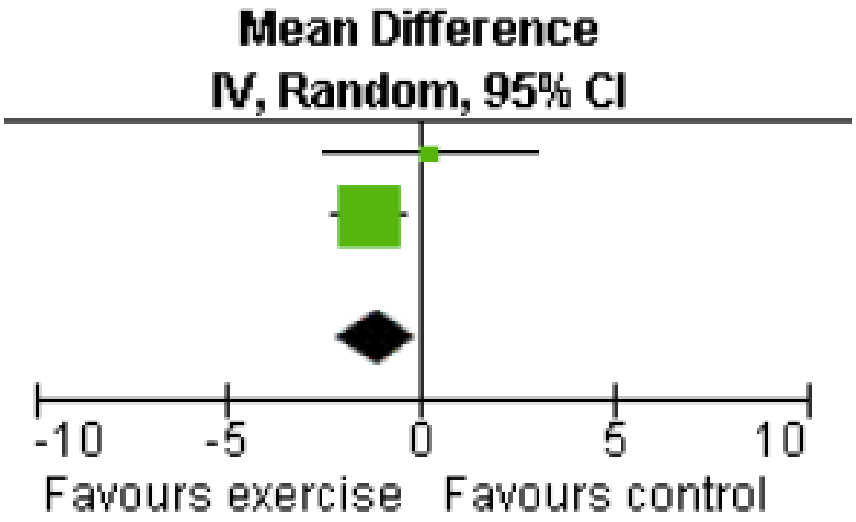
Constant aerobic exercise compared with no exercise. Outcome VO2max



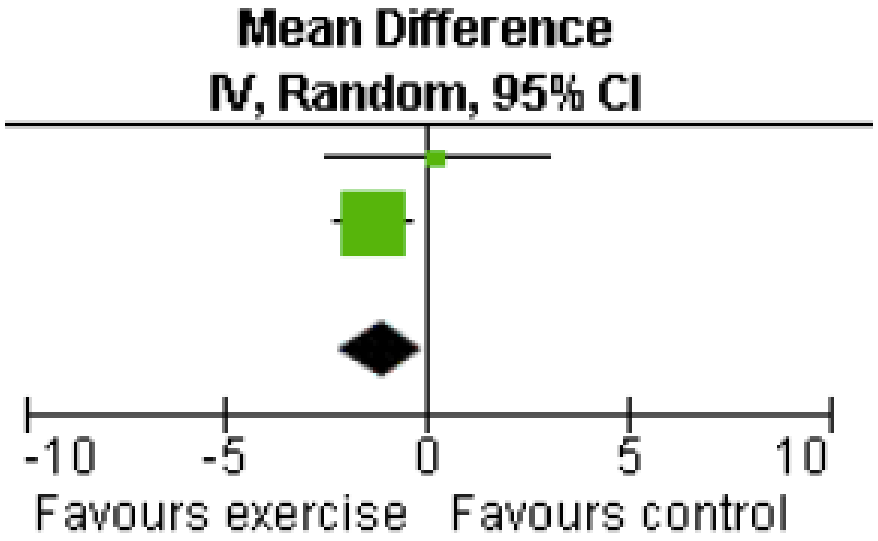
O'Brien et al. "Aerobic exercise interventions for adults living with HIV/AIDS (Review)". Cochrane collaboration. 2010

Significant decrease in body fat with regular exercise

Constant or interval aerobic exercise compared with no exercise. Outcome Body Fat %



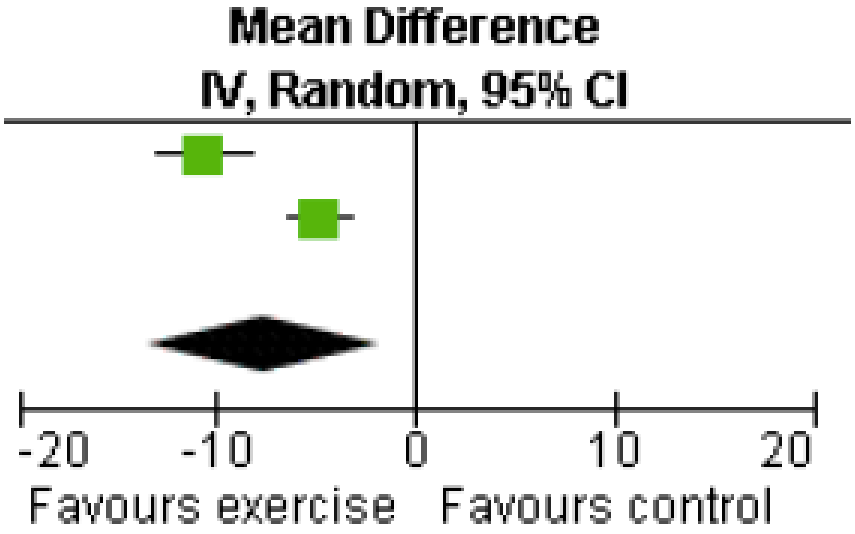
Constant aerobic exercise compared with no exercise. Outcome Body Fat %



O'Brien et al. "Aerobic exercise interventions for adults living with HIV/AIDS (Review)". Cochrane collaboration. 2010

Clinically important improvement in depression

Constant or interval aerobic exercise compared with no exercise. Outcome: POMS depression – dejection subscale



O'Brien et al. "Aerobic exercise interventions for adults living with HIV/AIDS (Review)". Cochrane collaboration. 2010

Effects of aerobic exercise on cognitive function - non-HIV populations

"**Dose-response Relationship between Exercise Duration and Cognition**"

- Twenty-six healthy young men
- Exercise at moderate intensity for 20 minutes resulted in significantly better cognitive performance as assessed by shorter response time and higher accuracy on the Stroop Test

Chang et al., 2014, *MSSE*.

Beneficial effects of aerobic exercise for those without mild cognitive impairment

“Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment.”

- … beneficial for cognitive function … with effects observed for motor function, cognitive speed, delayed memory functions and auditory and visual attention.

Angevaren et al., Cochrane Database Syst Rev. 2008

Beneficial effects of aerobic exercise for those with mild cognitive impairment

“Non-Pharmacological Interventions for Patients with Mild Cognitive Impairment: A Meta-Analysis of Randomized Controlled Trials of Cognition-Based and Exercise Interventions.”

- Both of cognition-based intervention and physical exercise had the potential to improve global cognitive function.

Wang et al., Journal of Alzheimer’s Disease, 2014.

Cross sectional data on fitness and HAND

"Poor aerobic fitness may contribute to cognitive decline in HIV-infected older adults"

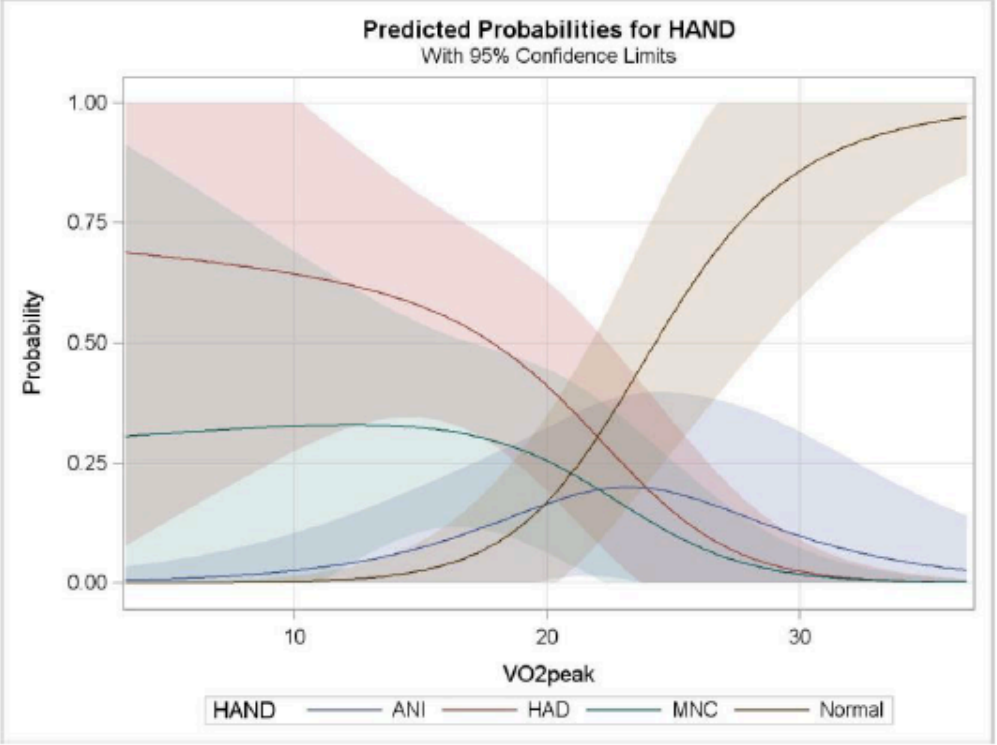


Figure 1. Predicted probabilities (with 95% Confidence Intervals) of cognitive impairment, based on aerobic fitness. Study participants were classified as cognitively normal, or as having a HAND diagnosis (ranging in severity from ANI [least severe], to MNC to HAD [most severe]. The curves demonstrate increasing probability of cognitive impairment with lower VO_{2peak} and increasing probability of better cognition with higher VO_{2peak}. The inflection point for classification appears to be around 22 ml/kg/min.

Mapstone et al., Aging and Disease 2013

Cross sectional studies on physical activity and HAND

"Physical exercise is associated with less neurocognitive impairment among HIV infected adults"

Defour et al., J Neurovirol. 2013

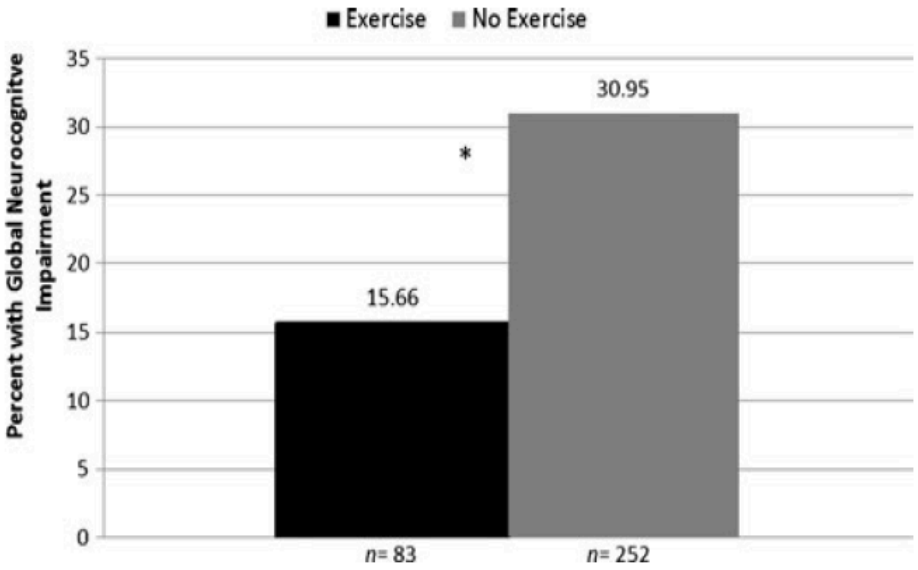
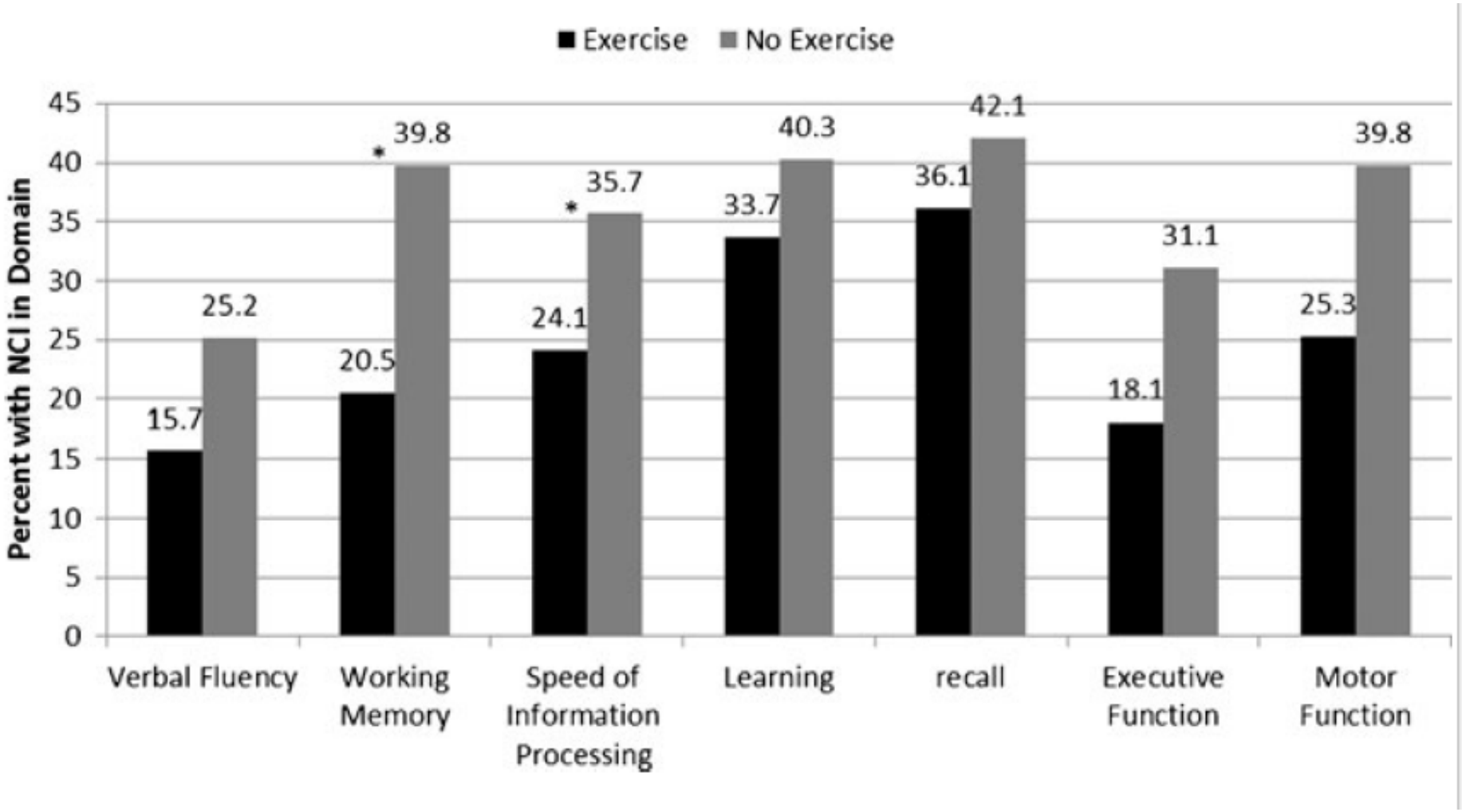


Fig. 1 HIV-infected persons who have not exercised in the last 72 h have double the neurocognitive impairment rate of those who have exercised. Note: Statistical significance (*$p<0.05$) derived from multivariable logistic regressions modeling impairment in each domain by group and adjusting for potential confounds

Subscales



Defour et al., J Neurovirol. 2013

- 16 week aerobic exercise programme improves sleep quality, results in structural changes in the hippocampus and trends towards improvements in inflammatory markers/immunity among HIV-negative sedentary volunteers
- HIV studies
  - 16 week aerobic exercise intervention (and control non-exercise group) with people living with HIV who have been diagnosed with HAND
  - Measurements: Fitness, Physical Activity, Sleep quality, Mood, QoL, Cognitive Function

- Understanding health, ageing and disease
- Advancing active and healthy ageing
- European Innovation Partnership on Active & Healthy Ageing

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