Increased and accelerated age-related complications in HIV-infected patients

Giovanni Guaraldi
Università di Modena
THE CHANGING SPECTRUM OF HIV CARE

1996
Pre-HAART
Opportunistic infections
AIDS cancers

Early-HAART
Lipodystrophy
Co-morbidities

Late-HAART
Multimorbidity
Frailty & Disability

2005
High prevalence of Co-morbidities (HANA) and Polypathology in HIV infected aging cohorts

In Modena cohort Pp on the 50’s was 20% in the AgeHIV cohort was 35% Pp prevalence was higher in cases than controls in all age strata

Schouten J, XIX International AIDS Conference
Accentuated Aging: cancer (and geriatric syndroms) occurs at the same ages but more often among HIV-infected participants than among HIV-uninfected comparators. This configure a Premature aging process.

Accelerated Aging and accentuated aging: cancer (and geriatric syndroms) occurs earlier among HIV-infected participants compared with HIV-uninfected comparators and there are more cancer events.
Age at Cancer Diagnosis Among Persons With AIDS in the United States

Age distribution in the AIDS and general populations

Standardized incidence ratios (SIRs), were calculated as the number of observed cases in the AIDS population divided by the number of expected cases in the general population, adjusted for the underlying population structures.
Potential covariates and Confounders

**Demographics**
Age, gender, ethnicity, yrs education, socio-economic, un/employment, etc.

**NeuroPsych**
HAND, dementia, depression, disposition/mood, substance ab/use, etc

**Medical-Physion**
Other meds, cardiometabolic risk, hepatorenal status, cancer BMD, lat/lean, endocrine and inflammatory markers, lifestyle, tobacco, rec. drugs, diet, physical inactivity, ADL, IADL, etc.

**HIV Related**
Yrs HIV, AIDS dx, HIV med compliance-complication, CD4, plasma and CSF viremia, immune activation, co-infections, chronic inflammation, etc.

**Social Vulnerability aspects**
Poverty, food security, Access to care, social justice, etc.
At any age, long-term infected people (ageing patients) had a 5-fold accentuated risk of multimorbidity than HIV-negative controls, while more recently infected people (aged patients) had an intermediate risk compared with the control group.
Future challenges for clinical care of an ageing population infected with HIV: a modelling study

Mikaela Smit, Kees Brinkman, Suzanne Geerlings, Colette Smit, Kalyani Thyagarajan, Ard van Sighem, Frank de Wolf, Timothy B Hallett, on behalf of the ATHENA observational cohort

- In the ATHENA cohort, proportion of patients on ART aged ≥50 years old will increase from 28% to 73% between 2010 and 2030
- Burden of NCDs mostly driven by larger increases in cardiovascular disease compared with increases in other comorbidities
A geriatric definition of old-Age:
65-75 YRS: Youngest old
76-84 YRS: Old
>85: Oldest-old

Corriere della sera, 25 maggio 2016
Frailty has been proposed as a measure of biological (opposed to chronological) aging.

This variable vulnerability among people of the same chronological age is known as frailty.
WYSIWYG!
What you see, is what you get

Frailty as a deficit accumulation

- Frailty can be operationalized as deficit accumulation and can be expressed in a frailty index
- Can be summarised as a scale from Robust to Terminally Ill
- A frailty index derived from routinely collected clinical data can offer insights into the biology of aging using mathematics of complex systems

Rockwood et al. Lancet 1999;353:205-6
Trajectories of physical function in older subjects

- Robust
- Frail and pre-frail (Reversible)
- Disable (ADL-Mobility Dependence)

**Aging “Normal”**

- **Aging “Accelerated”**

**ADL-Mobility Disability**

- Physical Function
- Age (years)
Objective

We aimed to estimate levels of Frailty and its implications for HIV care in Italy up to 2030.

Falls and Instrumental Activities of Daily Living (IADL) were used as proxy of geriatric syndromes and disability in the geriatric population.
Methods

✓ Geriatric age categories were chosen: <35, 35-49, 50-64, 65-75, >75

✓ An individual-based model of the ageing population of the Modena HIV Metabolic Clinic cohort (MHMC) was constructed using data collected between 2009 and 2015 from 2982 patients.

✓ The model follows patients enrolled to the clinic up to 2015 and generates new entries on a yearly basis up to 2030. Number, age and gender of new entries were modelled using trends observed in the period 2009-2015.

✓ The relationship between age and gender, falls and disability, observed in 2014-2015 at MHMC was postulated to constant over time.
Distribution of frailty index scores at first visit. Bars represent 0.01 frailty index score groupings. Solid line indicates normal distribution.

Average frailty index score at each age. Lines represent exponential best fit. Solid line is men, dashed line is women.

## Results

Socio-demographic, anthropometric and lifestyle characteristics

<table>
<thead>
<tr>
<th></th>
<th>HIV-positive (N=2982)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>951 (31.9%)</td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>49 (45, 54)</td>
</tr>
<tr>
<td>BMI (kg/m^2), median (Q1, Q3)</td>
<td>23.5 (21.4, 26.0)</td>
</tr>
<tr>
<td>Waist (cm), median (Q1, Q3)</td>
<td>87 (81, 94)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
</tr>
<tr>
<td>No smoking</td>
<td>1756 (58.9%)</td>
</tr>
<tr>
<td>1-10 cigarettes per day</td>
<td>516 (17.3%)</td>
</tr>
<tr>
<td>&gt;10 cigarettes per day</td>
<td>672 (22.5%)</td>
</tr>
</tbody>
</table>
## HIV-specific characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>HIV-positive (N=2982)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely route of transmission, n (%)</td>
<td></td>
</tr>
<tr>
<td>Homosexual sex</td>
<td>881 (29.5%)</td>
</tr>
<tr>
<td>CDC classification “C”, n (%)</td>
<td>699 (23.4%)</td>
</tr>
<tr>
<td>Years since HIV diagnosis, median (Q1, Q3)</td>
<td>19.7 (12.8, 24.4)</td>
</tr>
<tr>
<td>Currently on cART, n (%)</td>
<td>2810 (92.5%)</td>
</tr>
<tr>
<td>Duration of cART (years), median (Q1, Q3)</td>
<td>5.2 (2.6, 7.8)</td>
</tr>
<tr>
<td>Currently on NRTIs, n (%)</td>
<td>2319 (82.5%)</td>
</tr>
<tr>
<td>Currently on PIs, n (%)</td>
<td>1550 (55.2%)</td>
</tr>
<tr>
<td>Currently on NNRTIs, n (%)</td>
<td>1103 (39.3%)</td>
</tr>
<tr>
<td>Currently on other drugs, n (%)</td>
<td>569 (20.6%)</td>
</tr>
<tr>
<td>CD4 count (cells/µL), median (Q1, Q3)</td>
<td>648 (474, 841)</td>
</tr>
<tr>
<td>Nadir CD4 count (cells/µL), median (Q1, Q3)</td>
<td>200 (86, 300)</td>
</tr>
</tbody>
</table>
## Prevalence of comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>MHMC (N=2982)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease, n (%)</td>
<td>142 (4.8%)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>1088 (36.5%)</td>
</tr>
<tr>
<td>Impaired Fasting Glucose, n (%)</td>
<td>602 (20.2%)</td>
</tr>
<tr>
<td>Type 2 Diabetes, n (%)</td>
<td>393 (13.2%)</td>
</tr>
<tr>
<td>Lipodystrophy, n (%)</td>
<td>2265 (76.0%)</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>2449 (82.1%)</td>
</tr>
<tr>
<td>NAFLD, n (%)</td>
<td>701 (23.5%)</td>
</tr>
<tr>
<td>Renal Insufficiency, n (%)</td>
<td>284 (9.5%)</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>28 (0.9%)</td>
</tr>
<tr>
<td>Liver cirrhosis, n (%)</td>
<td>352 (11.8%)</td>
</tr>
<tr>
<td>Vitamin D insufficiency, n (%)</td>
<td>2061 (69.1%)</td>
</tr>
<tr>
<td>Osteoporosis, n (%)</td>
<td>269 (9%)</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>91 (3.1%)</td>
</tr>
<tr>
<td>Any AIDS malignancy, n (%)</td>
<td>77 (2.6%)</td>
</tr>
</tbody>
</table>
# Prevalence of comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>MHMC (N=2982)</th>
<th>ATHENA (N=10278)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease, n (%)</td>
<td>142 (4.8%)</td>
<td>372 (4%)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>1088 (36.5%)</td>
<td>2379 (23%)</td>
</tr>
<tr>
<td>Impaired Fasting Glucose, n (%)</td>
<td>602 (20.2%)</td>
<td></td>
</tr>
<tr>
<td>Type 2 Diabetes, n (%)</td>
<td>393 (13.2%)</td>
<td>578 (6%)</td>
</tr>
<tr>
<td>Lipodystrophy, n (%)</td>
<td>2265 (76.0%)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>2449 (82.1%)</td>
<td></td>
</tr>
<tr>
<td>NAFLD, n (%)</td>
<td>701 (23.5%)</td>
<td></td>
</tr>
<tr>
<td>Renal Insufficiency, n (%)</td>
<td>284 (9.5%)</td>
<td></td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>28 (0.9%)</td>
<td>1399 (14%)</td>
</tr>
<tr>
<td>Liver cirrhosis, n (%)</td>
<td>352 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>Vitamin D insufficiency, n (%)</td>
<td>2061 (69.1%)</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis, n (%)</td>
<td>269 (9%)</td>
<td>829 (8%)</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>91 (3.1%)</td>
<td></td>
</tr>
<tr>
<td>Any AIDS malignancy, n (%)</td>
<td>77 (2.6%)</td>
<td>765 (7%)</td>
</tr>
</tbody>
</table>
Observed (red area) and projected age distribution of HIV-infected patients

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2016 Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>3.8%</td>
</tr>
<tr>
<td>35-49</td>
<td></td>
</tr>
<tr>
<td>50-64</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td></td>
</tr>
<tr>
<td>&gt;75</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Geriatric Age categories:
- 65-74 yrs
- >74 yrs

Proportion of people (%)
Observed (red area) and projected age distribution of HIV-infected patients

Age
- <35
- 35-49
- 50-64
- 65-74
- >75

Geriatric Age categories
- 65-7 yrs
- >74 yrs

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;35</th>
<th>35-49</th>
<th>50-64</th>
<th>65-74</th>
<th>&gt;74 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>3.8%</td>
<td>0.5%</td>
<td>57.2%</td>
<td>37.4%</td>
<td>0.5%</td>
</tr>
<tr>
<td>2020</td>
<td>5.7%</td>
<td>0.8%</td>
<td>59.5%</td>
<td>34.7%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>
Observed (red area) and projected age distribution of HIV-infected patients

<table>
<thead>
<tr>
<th>Age category</th>
<th>2016</th>
<th>2020</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>3.8%</td>
<td>5.7%</td>
<td>14.4%</td>
</tr>
<tr>
<td>35-49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;75</td>
<td>0.5%</td>
<td>0.8%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>
In 15 years time the HIV geriatric population will increase from 4% to 37%.
Observed (red area) and predicted burden of Frailty in HIV-infected patients between 2009 and 2030 as simulated by the model

In 15 years time the most frail HIV population will increase from 24% to 48%
Male

2002
39 yrs

2015
50 yrs

2016
51 yrs

CD4=477 cells/µL
HIV1-RNA<40 copies/mL
TDF+FTC+NEV

CD4=715 cells/µL
HIV1-RNA<40 copies/mL
TDF+FTC+NEV

CD4=357 cells/µL
HIV1-RNA non detectable
RAL+NEV
PATIENT AGEING TRAJECTORY

Drug toxicities  Co-morbidities  Multi-morbidities  Frailty  Disability

Impairment (body function): Osteoarthritis

Limitations (activity): Slow chair rise time, slow gait

Frailty (vulnerability): Slow walking speed, low activity, fatigue

Disabilities (participation): Requires cane, but ramp into home and no stairs in home

Impairment: History, exam, X-ray

Limitations: Short Physical Performance Battery
Timed walk

Frailty: Fried's frailty phenotype

Disability: Activities of daily living
Independent activities of daily living

In HIV+ older adults, IADL impairment occurs more frequently among those with neuroimpairment or frailty.

Modifiable risk factors (smoking, low physical activity) provide targets for interventions to help maintain independent living.

Erlandosn K, P-721 CROI 2016
**Geriatric Syndromes in Older HIV-Infected Adults**

Meredith Greene, MD,*† Kenneth E. Covinsky, MD, MPH,*† Victor Valcour, MD, PhD,*‡ Yinghui Miao, MD, MPH,*† Joy Madamba, BS,§ Harry Lampiris, MD,#‖ Irena Stijacic Cenzer, MA,*† Jeffrey Martin, MD, MPH,¶ and Steven G. Deeks, MD§

**FIGURE 1.** Frequencies of geriatric syndromes. Each bar reflects the percentage of participants with each geriatric syndrome. Actual percentages are shown at the end of each bar. Horizontal axis only shown to 60%.
Observed (red area) and predicted burden of Falls in HIV-infected patients between 2009 and 2030 as simulated by the model

In 15 years time 30% of PLWH will experience a geriatric syndrome
Observed (red area) and predicted burden of IADL in HIV-infected patients between 2009 and 2030 as simulated by the model.

In 15 years time 34% of PLWH will be disable.
How to manage HIV as a chronic condition

- Opt-out HIV screening in all adults, regardless of age or individual factors\(^1\)
- Detection and screening for HIV in older adults\(^1\)
- Functional status assessment
- Self reported and performance based morbidity assessment
- Reduce risks of polypharmacy\(^1\)
- Toxicity
  - Drug-drug interactions
  - Adherence issues\(^1\)
- Social support & Promote lifestyle changes\(^2-4\)
- Obtain undetectable VL
- Screening for co-morbidities & risk factors\(^1\)
- Consider co-morbidities in choosing ART\(^1\)
- Healthy diet
  - Smoking cessation
  - Increase physical activity
  - Sexual health counseling\(^2-4\)

*if plasma HIV RNA levels > 50,000 copies/ml, greater than 100-point decline in CD4 count in prior 12 months, or risk factors for CVD.

Healthy life expectancy is a measure that combines mortality and morbidity information in one index, expressing the number of healthy years of life lost because of poor health, and incorporating a range of severities to quantify poor health.

Data from the Global Burden of Disease 2010 show that from 1990 to 2010, as life expectancy rose 20 years healthy life expectancy increased more slowly (0.75 years for each year of increase in life expectancy).
The chronic care model is a guide to higher-quality chronic illness management within primary care. The model predicts that improvement in its 6 interrelated components—self-management support, clinical information systems, delivery system redesign, decision support, health care organization, and community resources—can produce system reform in which informed, activated patients interact with prepared, proactive practice teams. Case studies are provided describing how components of the chronic care model have been implemented in the primary care practices of 4 health care organizations.
Improving Primary Care for Patients With Chronic Illness

The Chronic Care Model

- **Community**
  - Resources and Policies
  - Self-Management Support

- **Health Systems**
  - Organization of Health Care
    - Delivery System Design
    - Decision Support
    - Clinical Information Systems

- **Informed, Activated Patient**
- **Prepared, Proactive Practice Team**
- **Productive Interactions**

**Improved Outcomes**

Developed by The MacColl Institute
Delivery System Design: Assure the delivery of effective, efficient clinical care and self-management support

- HIV physicians
- Psychologist
- Nurse
- Occupational therapist
- Pharmacist
- Non HIV specialists

Multidimensional assessment of HEALTH

Mental Health

Improved Outcomes

Beyond HIV undetectability

HIV beyond undetectability

Mental Health

QoL

Occupational therapy

Physical function

Physical function

Geriatric syndromes

Disability
CLINICAL MANAGEMENT: Health care organization & Delivery system design
Decision Support: Promote clinical care that is consistent with scientific evidence and patient preferences.

HIV & hepatitis drug interactions

- [http://www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)
- [http://www.hep-druginteractions.org](http://www.hep-druginteractions.org)
Clinical Information Systems: Organize patient and population data to facilitate efficient and effective care.

Successful Aging... beyond the absence or regardless co-morbidities and HIV.

Measure of disease:

T0  T18mts

Measure of Health

mySawh
Clinical Information Systems: Organize patient and population data to facilitate efficient and effective care.

Successful Aging... beyond the absence or regardless co-morbidities and HIV.
Clinical Information Systems:
Organize patient and population data to facilitate efficient and effective care

Successful Aging... beyond the absence or regardless co-morbidities and HIV

Measure of disease
Clinical Information Systems: Organize patient and population data to facilitate efficient and effective care.

Successful Aging... beyond the absence or regardless co-morbidities and HIV.

Physiologic data (steps, sleep, calories)

T0 to T18mts

mymireh
Clinical Information Systems:
Organize patient and population data to facilitate efficient and effective care

Successful Aging... beyond the absence or regardless co-morbidities and HIV
Clinical Information Systems: Organize patient and population data to facilitate efficient and effective care

Successful Aging... beyond the absence or regardless co-morbidities and HIV

Frailty Index

Measure of disease

Health Index

Measure of Health

The Chronic Care Model

Community

Health Systems

Clinical Information Systems

Improved Outcomes

Informed, Activated Patient

Productive Interactions

Prepared, Proactive Practice Team

Delivery System Design

Decision Support

T0

T18mts
Health Index

Neurocognitive

Mood

Social Vulnerability

Statistiche paziente: 2842
The community: Mobilize community resources to meet needs of patients
The Multiple Stigma Experience and Quality of Life in Older Gay Men With HIV

Take home message (1/2)

• Comorbidities are the prevalent clinical picture of contemporary HIV disease
• The association of comorbidities into complex multi-morbidity pictures describe patient complexity
• When Multi-morbidity is the norm, frailty and disability turn to be relevant clinical outcomes and allows patient risk stratification beyond the CD4 and HIV VL assessment
• Total patient care allows to integrate the need for reaching undetectability with the need to take care of comorbidities.
Take home message (2/2)

- HIV Care implies a switch from a Inter-disciplinary approach into a Multi-dimensional comprehensive assessment
- Patient visit diversification must be built in an individualised management plan focused on quality of life and prevention of disability
- The increasing numbers of older patients with frailty, geriatric syndromes and disability depict an “geriatric -HIV” scenario. This model suggests evidence-based screening and monitoring protocols to ensure high-quality care.
The new target

90-90-90-90-90

90% diagnosed
90% on treatment
90% virally suppressed

90% fit at 90 years

Thank you....
...and stay fit!