Emerging issues in HIV treatment: A clinical perspective on HIV and aging

Marta Boffito
Emerging issues in HIV treatment: A clinical perspective on HIV and aging

Prof Marta Boffito MD, PhD, FRCP, MBA

Consultant Physician
Clinical Director - HIV, Sexual and Gender Health, Dermatology
Chelsea and Westminster Hospital NHS Foundation Trust
Imperial College London

London, UK
Disclosures:

Travel grants
Speaker
Advisor
Research grants

Janssen, Roche, ViiV, Bristol-Myers Squibb, MSD, Gilead, Mylan, Cipla, Novavax, Valneva, GSK, Pfizer, AZ, ATEA
Outline

• My experience of delivering care to people ageing with HIV

• Data and clinical concerns

• Quality of life

• Care models: HIV and ageing
A dedicated clinic for the over 50’s at CWH – today a pathway for all PLWH > 50

Data from the HIV over 50 clinic:
- Showed high rates of comorbidities and polypharmacy
- Led to the implementation of clinical care pathways for all HIV care providers
- Led to the set up of new joint HIV/specialty clinics (cardiology, nephrology, neurology, metabolic, menopause, and geriatric)
- Helped improve prevention, diagnosis, and management of comorbidities and polypharmacy
Co-morbidities are prevalent among ageing people living with HIV

**AANCC incidence stratified by age in the AGE$_{h}$IV Cohort Study, 2010–2012**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>45–49</th>
<th>50–54</th>
<th>55–59</th>
<th>60–64</th>
<th>≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of AANCC</td>
<td>0.83</td>
<td>1.18</td>
<td>1.34</td>
<td>1.52</td>
<td>1.96</td>
</tr>
<tr>
<td>Number of participants</td>
<td>184</td>
<td>126</td>
<td>97</td>
<td>58</td>
<td>55</td>
</tr>
</tbody>
</table>

HIV-infected (N=540)
Mean AANCC/person = 1.3 (SD 1.14)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>45–49</th>
<th>50–54</th>
<th>55–59</th>
<th>60–64</th>
<th>≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of AANCC</td>
<td>0.79</td>
<td>0.75</td>
<td>1.11</td>
<td>1.08</td>
<td>1.51</td>
</tr>
<tr>
<td>Number of participants</td>
<td>193</td>
<td>130</td>
<td>84</td>
<td>66</td>
<td>41</td>
</tr>
</tbody>
</table>

HIV-uninfected controls (N=524)
Mean AANCC/person = 1.0 (SD 0.96)
Do patients with HIV age prematurely?

- Increasing age, ageing process
- Drug toxicity e.g. TDF and Nephrotoxicity
- Lifestyle (drugs, alcohol)
- Persistent immune dysfunction and inflammation

Do patients with HIV age prematurely?

- Metabolic syndrome
- Neurological impairments
- Cancer
- Bone disease
- Liver disease
- Kidney disease
- CVD

Polypharmacy

- Definition: use of ≥5 medications\(^1\)
- Increased medication use is associated with\(^1\):
  - ↓ adherence and ↑ pill fatigue
  - ↑ risk of adverse drug events
  - ↑ drug–drug and drug–disease interactions
  - Geriatric syndromes (eg, falls, cognitive impairment, frailty)
  - Mortality
- Polypharmacy is one of the strongest predictors of serious ADEs,\(^2\) drug–drug interactions,\(^2\) and fall risk\(^3\)
- Dose–response association with all-cause and CVD mortality\(^4\)

POPPY Study: Polypharmacy and drug interactions in Older people with HIV

Compared to HIV-negative controls or younger PWH, older PWH were more likely:

- To have polypharmacy, even when ARVs were excluded
- To be at risk of a PDDI involving non-ARV/ARV drugs

Results highlight the need for increased awareness and additional research around polypharmacy and all PDDI

Age (years), Median (range) | PLWH aged >50 years | PLWH aged <50 years | HIV-negative controls aged >50 years | P-Value
---|---|---|---|---
56 (50-82) | 43 (20-49) | 58 (50-87) | 0.001

Total number of medication
Median (range) | 6 (0-27) | 4 (0-17) | 1 (0-39) | 0.001
n (%) with PP | 459 (65.3%) | 180 (48.1%) | 40 (13.2%) | 0.001

PDDI between non-ARV drugs
n (%) ≥1 | 252 (36.1%) | 76 (20.3%) | 49 (16.1%) | 0.001
Median (range) | 0 (0-48) | 0 (0-21) | 0 (0-14) | 0.001

% on ARVs | 98.7% | 95.2% | - | -

PDDI between ARV & non-ARV drugs
n (%) ≥1 | 398 (57.3%) | 121 (32.4%) | - | 0.001
Median (range) | 1 (0-11) | 0 (0-5) | - | 0.001

Number of medications Excluding ARVs in PWH

O Halloran et al. Antiviral Ther 2019
**General De-Prescribing**

**ART**
- VL undetectable
- ARV history & archived resistance testing results support alternative options
- Lower DDI and toxicity
- Maintain undetectable VL

**Non-ART**
- Supervised by a health care professional
- Goal = managing polypharmacy/reduce risks and improving outcomes
- Discontinue inappropriate meds
- Use evidence that is feasible and safe

Guaraldi et al. JAC 2020; Blanco et al Eur J Clin Pharmacol 2020
Recent evidence on cardiometabolic outcomes

<table>
<thead>
<tr>
<th>OUTCOME MEASURE</th>
<th>AUTHOR</th>
<th>PUBLICATION/PRESENTATION</th>
<th>YEAR</th>
<th>N</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI</strong></td>
<td>Bansi-Matharu et al.</td>
<td>Lancet HIV, 2021;September:S2352</td>
<td>2021</td>
<td>14703</td>
<td>Compared with 3TC; DTG (OR 1.27), RAL (OR 1.37), and TAF (OR 1.38) were significantly associated with more than 7% BMI increase</td>
</tr>
<tr>
<td><strong>DYSLIPIDEMIA</strong></td>
<td>Byonanebye DM et al.</td>
<td>AIDS 2021, 35:869–882</td>
<td>2021</td>
<td>4577</td>
<td>Participants taking InSTI had a lower incidence of dyslipidemia compared with those on PI/b (adjusted IRR 0.71), but higher rate compared with those on NNRTI (1.35).</td>
</tr>
<tr>
<td><strong>HYPERTENSION</strong></td>
<td>Byonanebye DH et al.</td>
<td>HIV Med. 2022 Mar</td>
<td>2022</td>
<td>4606</td>
<td>PLWH receiving InSTI had a 76% higher incidence of HTN than those receiving NNRTIs (aIRR=1.76)</td>
</tr>
<tr>
<td><strong>DIABETES MELLITUS</strong></td>
<td>Byonanebye DH et al.</td>
<td>IAS2023 OALBB0505</td>
<td>2023</td>
<td>9704</td>
<td>Impact of INSTI and TAF-related BMI changes and risk on hypertension and dyslipidemia in RESPOND</td>
</tr>
<tr>
<td><strong>NAFLD</strong></td>
<td>O’Halloran JA et al.</td>
<td>CID, 2022; ciac355, <a href="https://doi.org/10.1093/cid/ciac355">https://doi.org/10.1093/cid/ciac355</a></td>
<td>2022</td>
<td>42382</td>
<td>PWH starting an InSTI were 31% more likely to develop DM vs. those starting a non-INSTI (NNRTI or PI)</td>
</tr>
<tr>
<td><strong>NAFLD</strong></td>
<td>Bischoff J, et al.</td>
<td>EClinicalMedicine. 2021 Sep 5;40:101116</td>
<td>2021</td>
<td>319</td>
<td>A BMI&gt;23 kg/m² (OR: 4.24), TAF (OR: 5.07); and InSTI (OR: 2.35), as well as type 2 DM (OR: 7.61) were independent predictors of de novo steatosis in multivariable analysis</td>
</tr>
<tr>
<td><strong>CV EVENTS</strong></td>
<td>Neesgaard et al.</td>
<td>Lancet HIV. 2022 Jun 7:S2352-3018(22)00094-7.</td>
<td>2022</td>
<td>29340</td>
<td>InSTI exposure was associated with an aIRR of 1.85 for CVD events in the first 6 months after InSTI initiation compared with no exposure</td>
</tr>
<tr>
<td><strong>CV EVENTS</strong></td>
<td>Donga et al</td>
<td>AIDS2022 EPB108</td>
<td>2022</td>
<td>14076</td>
<td>Patients initiating InSTI were significantly more likely to experience congestive heart failure (HR=2.12), myocardial infarction (HR=1.79), and lipid disorders (HR=1.26) than those initiating non-InSTI.</td>
</tr>
</tbody>
</table>
The Fourth 90 (or 95): Quality of Life, Not Just Quantity of Life

“90-90-90” target championed by UNAIDS

- 90% Diagnosed
- 90% On treatment
- 90% Virally suppressed
- 90% Good health-related quality of life

The ‘fourth 90’:
To ensure that 90% of people with viral load suppression have a good health-related QoL

QoL, quality of life; UNAIDS, The Joint United Nations Programme on HIV/AIDS.
The Fourth 90 (or 95): Quality of Life, Not Just Quantity of Life

“How can clinical and scientific knowledge contribute to the achievement of health equity by eliminating health disparities and achieving optimal health for all?”

Health equity is achieved when every person has the opportunity to “attain his or her full health potential” and no one is “disadvantaged ... Health inequities are reflected in differences in length of life; quality of life; rates of disease, disability, and death; severity of disease; and access to treatment.”

“90-90-90” target championed by UNAIDS

Health equity is achieved when every person has the opportunity to “attain his or her full health potential” and no one is “disadvantaged ... Health inequities are reflected in differences in length of life; quality of life; rates of disease, disability, and death; severity of disease; and access to treatment.”

Implementation of new models of care

Geriatric care
- Behavioral Health
  E.g., Substance use, insomnia

HIV care
- Existential
  E.g., loneliness, fear
- Mental Health
  E.g., depression, anxiety

Primary care
- Practical needs
  E.g., nutrition, housing
- Social stressors
  E.g., stigma, isolation
Mental Health Impairment Contributes to Poorer Outcomes

- All lead to non-optimal HIV treatment and poorer health outcomes (for self and for others)
- Whatever the pathway, it is clear that we need to address mental health problems if we want to improve health outcomes along the HIV prevention and HIV care continua

Benefits of Integrating Mental Health Screening and Treatment into HIV Care

First critical step

MH care integration

- Reduced HIV Risk Behaviour
- Improved Adherence to HIV Care and Treatment
- Improved Linkage and Retention
- Reduction in HIV Transmission
- Treating depression improves adherence
- Reduced Viral Load

Improvements in Mediators:
- Mental health symptoms
- Substance use
- Stress and coping

Reduced HIV Risk Behaviour

Image adapted from Sikkema KJ et al. 2010.

HIV, human immunodeficiency virus; MH, mental health; PTSD, post-traumatic stress disorder; SUD, substance use disorders

# Strengths and Challenges of Various Models of Geriatric Consultation for Older Adults Living With Human Immunodeficiency Virus

<table>
<thead>
<tr>
<th>Model Type</th>
<th>Overall Description</th>
<th>Institution Name</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: Outpatient referral/consultation</td>
<td>Referral to a geriatrician for recommendations to enhance a patient’s care plan; HIV provider remains as primary provider</td>
<td>Positive Aging Consultation, University of Colorado</td>
<td>Aurora, Colorado</td>
</tr>
<tr>
<td>Model 2: Combined HIV/geriatric multidisciplinary clinic</td>
<td>A multidisciplinary team is incorporated into existing HIV/infectious disease clinics to provide a comprehensive assessment and evaluation of each patient; primary care providers are provided with full evaluation and recommendations from the multidisciplinary team</td>
<td>The THRIVE Program; Comprehensive HIV and Aging Initiative of the Chronic Viral Illness Service, McGill University Hospital Center; Chelsea and Westminster Hospital [11]; Silver Clinic [12]; Golden Compass Program, University of California; San Francisco/Zuckerberg San Francisco General Hospital [14, 16]; Center for Special Studies, New York Presbyterian/Weill Cornell Medical Center [13, 15]</td>
<td>Baltimore, Maryland; Montreal, Quebec, Canada; London, United Kingdom; Brighton, United Kingdom; San Francisco, California; New York City, New York</td>
</tr>
<tr>
<td>Model 3: Dually trained providers</td>
<td>An HIV provider with an invested interest in geriatric care performs assessments and provides recommendations; Dually boarded provider: a single provider with both geriatric and HIV expertise in 1 clinical home</td>
<td>Age Positively Program, Massachusetts General Hospital; Penn Community Practice and Penn Geriatrics, University of Pennsylvania Medical Center</td>
<td>Boston, Massachusetts; Philadelphia, Pennsylvania</td>
</tr>
</tbody>
</table>

Challenges

- Knowledge on all the components of care
- Availability of HCPs
- Engagement from HCPs
- Engagement from service users
- Funding and sustainability
- Absence of guidelines
Conclusions

• Global population of older people with HIV growing
• Supporting healthy aging in stretched healthcare is challenging
• Older people with HIV deserve comprehensive healthcare: prevention, diagnosis, management of HIV, polymorbidity and polypharmacy
• New models of healthcare needed in both HIC and LMIC
• Learn from pilot programs, research, and models used in other fields (e.g., geriatrics)
• Implement local pathways
• Creation of guidelines