BHIVA guidelines for the management of HIV-2, 2020

“When to start” recommendations

Clare van Halsema, on behalf of the writing group

BHIVA virtual conference, November 2020

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Declaration of Interests relating to this presentation

- None

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When to start antiretroviral therapy

Key differences between “when to start” for HIV-1 and for HIV-2

- No “START study” for HIV-2: no randomised trials of timing of ART

- Lower viral loads than HIV-1 in general
- Many (25 – 40%) have undetectable HIV-2 RNA without ART

    - hence lower horizontal and vertical transmission risk than HIV-1
    - and slower disease progression

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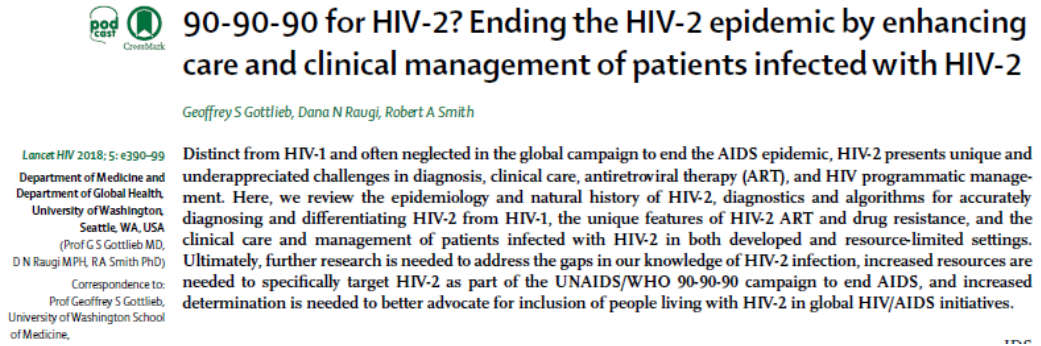
When to start antiretroviral therapy

And key similarities

- Opportunistic infections and clinical presentation are the same
- We assume that U=U
- 90-90-90 targets apply
- Stigma is likely to be the same



90-90-90 for HIV-2? Ending the HIV-2 epidemic by enhancing care and clinical management of patients infected with HIV-2

Geoffrey S Gottlieb, Dana N Raugi, Robert A Smith

Lancet HIV 2018; 5: e390–99

Department of Medicine and Department of Global Health, University of Washington, Seattle, WA, USA
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Prof Geoffrey S Gottlieb, University of Washington School of Medicine,

Distinct from HIV-1 and often neglected in the global campaign to end the AIDS epidemic, HIV-2 presents unique and underappreciated challenges in diagnosis, clinical care, antiretroviral therapy (ART), and HIV programmatic management. Here, we review the epidemiology and natural history of HIV-2, diagnostics and algorithms for accurately diagnosing and differentiating HIV-2 from HIV-1, the unique features of HIV-2 ART and drug resistance, and the clinical care and management of patients infected with HIV-2 in both developed and resource-limited settings. Ultimately, further research is needed to address the gaps in our knowledge of HIV-2 infection, increased resources are needed to specifically target HIV-2 as part of the UNAIDS/WHO 90-90-90 campaign to end AIDS, and increased determination is needed to better advocate for inclusion of people living with HIV-2 in global HIV/AIDS initiatives.

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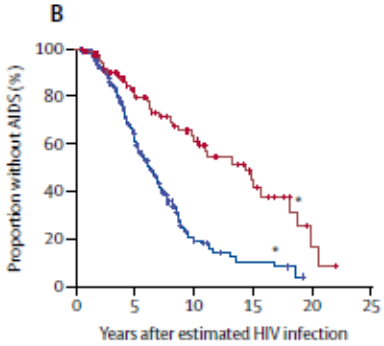
Evidence: recent cohort study example

Long-term follow-up of HIV-2-related AIDS and mortality in Guinea-Bissau: a prospective open cohort study

Joakim Esbjörnsson, Fredrik Månsson*, Anders Kvist, Zacarias J da Silva, Sören Andersson, Eva Maria Fenyö, Per-Erik Isberg, Antonio J Biague, Jacob Lindman, Angelica A Palm, Sarah L Rowland-Jones, Marianne Jansson, Patrik Medstrand, Hans Norrgren, the Sweden and Guinea-Bissau Cohort Research Group†*



Number at risk (number censored)						
HIV-1 infection	225 (0)	93 (66)	15 (96)	5 (101)	0 (104)	0 (104)
HIV-2 infection	87 (0)	52 (21)	31 (32)	13 (43)	2 (49)	0 (50)

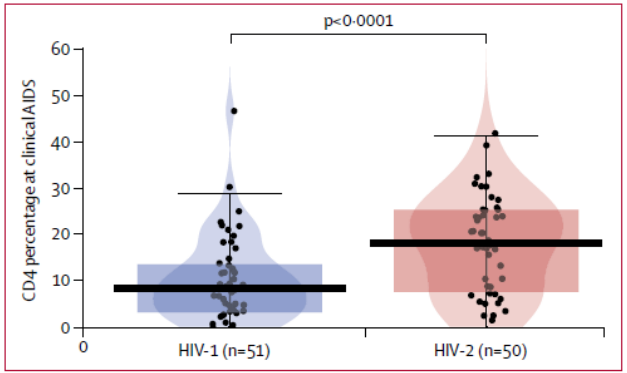


Figure 3: **Pirate plots of estimated CD4 percentages at clinical AIDS for HIV-1-infected and HIV-2-infected individuals**
Pirate plots combining individual observations (black points), box plots of the median, IQR, and 95% quantile range, as well as smoothed density distributions of the data are shown for each group. HIV-1=HIV type 1. HIV-2=HIV type 2.

- Occupational cohort, 1990 - 2013
- No viral loads, but good estimates of date of infection
- HIV-1/HIV-2/HIV negative comparisons
- Time to clinical AIDS 6.2 *vs* 14.3 years for HIV-1 vs HIV-2
- Minority started ART

Lancet HIV 2019; 6: e25–31

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Recommendations

Reminder of GRADE

Grading Recommendations Assessment, Development and Evaluation

Strength of recommendation	Strength/quality of evidence
1: "we recommend"	A: high
2: "we suggest"	B: moderate
	C: low
	D: very low
"GPP" = good practice point	

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Recommendations

- **It is essential that the risks and benefits of initiating ART are discussed with all individuals with HIV-2. (GPP)**
- **We suggest that all people with HIV-2 start ART. (Grade 2C)**

- **We recommend that people with HIV-2 start ART in the following circumstances:**
  - If there is dual HIV-1 and HIV-2 infection; (Grade 1A)
  - When a diagnosis is made during primary HIV-2 infection; (Grade 1C)
  - If there is co-infection with hepatitis B (HBV); (Grade 1C)
  - In pregnancy; (Grade 1C)
  - If there is detectable HIV-2 viraemia; (Grade 1B/C)
  - If the CD4 count is below 500 cells/mm^3; (Grade 1B)
  - In advanced HIV disease, or if there are opportunistic infections; (Grade 1B)
  - If there are symptoms, or an indicator condition for HIV-1 and/or HIV-2, regardless of CD4 count or viral load. (Grade 1C)

- **We suggest that additional consideration is given to starting ART if there are significant comorbidities. (Grade 2D)**

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We recommend that people with HIV-2 start ART if:

1. If there is dual HIV-1 and HIV-2 infection (1A)

Evidence in HIV-1 and the treatment recommendation is the same.

A treatment regimen should be designed that has fully suppressive activity against both viruses.

2. When a diagnosis is made during primary HIV-2 infection (1C)

Largely extrapolated from HIV-1: may reduce the reservoir of infected cells and likely to reduce risk of onward transmission

Clinical syndrome appears to be the same as primary HIV-1

3. If there is co-infection with hepatitis B (1C)

Extrapolation from evidence in HIV-1/hepatitis B co-infection

A treatment regimen should be designed that has fully suppressive activity against both viruses.

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We recommend that people with HIV-2 start ART if:

4. In pregnancy (1C)

Vertical transmission is a risk (not zero; 0.6 – 4%) and ART is likely to reduce that risk

Observational data on pregnancies in women with HIV-2 suggest ART effective

Start ART even if undetectable HIV-2 RNA, since this may change later in pregnancy

5. If there is detectable HIV-2 viraemia (1B)

Prevents disease progression (evidence in HIV-2)

Prevents onward transmission, as well as reducing the risk of non-AIDS adverse events (evidence in HIV-1).

Disease progression seen in HIV-2 with very low-level viraemia (CD4 matched viral load 10-100x lower than HIV-1), so viraemia is a strong indication to treat

6. If the CD4 count is below 500 cells/mm^3 (1B)

Disease progression is similar to (but slower than) in HIV-1 and opportunistic disease may be seen at higher CD4 counts

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We recommend that people with HIV-2 start ART if:

7. In advanced HIV disease, or if there are opportunistic infections (1B)

WHO definition: CD4 <200 cells/µL or WHO stage 3 or 4 clinical event

Some extrapolation from HIV-1, but ART does lead to improved CD4 counts in HIV-2

8. If there are symptoms, or an indicator condition for HIV-1 and/or HIV-2, regardless of CD4 count or viral load. (1C)

To improve symptoms and because symptoms may be markers of immunosuppression

We suggest that additional consideration is given to starting ART if there are significant comorbidities. (2D)

Higher mortality in >45s with HIV-2

Extrapolation from HIV-1

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We suggest that people with HIV-2 start ART (2C)

FOR

- CD4 count improvement seen in cohort studies
- Disease progression seen without ART, leading to advanced disease and death
- Opportunistic disease seen at higher CD4 counts in people with HIV-2 *vs* HIV-1
- Likely public health benefit, as U=U

AGAINST

- No randomised controlled trials to determine optimal timing of ART in HIV-2
- Cohort studies subject to confounding, many without viral load monitoring and not in high-income settings
- In cohort studies, 25-40% of ART-naïve individuals have undetectable HIV-2 RNA
- Long term follow up data including people with undetectable HIV-2 RNA off ART not available

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It is essential that the risks and benefits of initiating ART are discussed with all individuals with HIV-2. (GPP)

- Detailed discussion, perhaps more so than in HIV-1
- Ensure correct information given and explain differences between HIV-1 and HIV-2
- Consider benefits to engagement and retention in care of starting ART

GPP = good practice point

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