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Q&A on the impact of the interruption of treatment for people living with HIV

Background and purpose

UNAIDS data show that in 2023, 39.9 million people were living with HIV globally, of whom 53% were women and girls. An estimated 30.7 million people living with HIV were accessing antiretroviral treatment (ART), and almost three quarters (78% of women and 67% of men living with HIV) had a suppressed viral load.[1] According to UNAIDS, more than 25 million deaths have been averted since 2003 by ART.

Recent suspensions and reductions in official development assistance (ODA) have posed significant challenges to HIV programme continuity in several countries. These funding disruptions have impacted people living with HIV and other vulnerable populations who rely on these essential services, like antiretroviral treatment, particularly in settings reliant on external financing[2]. In some cases, governments are stepping in to reestablish services that were previously provided through other sources of funding.

In April 2025, WHO issued a public Q&A resource to help answer some of the questions and challenges posed by service disruptions[3]. Communities of people living with HIV are monitoring the extent of service disruptions and are offering advice and support to those affected. Several networks have issued helpful guidance for individuals who may run out of antiretrovirals (ARVs) and other medications, due to local or central drug stock ruptures and/or clinic closures.

When ART is stopped, HIV viral load can rise rapidly. This sustained increase of viral load progressively damages the immune system and heightens the risk of a variety of opportunistic infections, advanced HIV disease (AIDS) and death.[4] In addition, any ongoing replication of HIV in the presence of suboptimal levels of antiretroviral medicines in the body promotes viral mutations that confer drug resistance.[5]

How quickly does viral load increase after ART is stopped?

When ART is interrupted, the HIV viral load can rebound rapidly. The reported timelines of viral load rebound vary between individual and population studies. For most people, the viral load will reach baseline viral load (the viral load measure recorded prior to treatment initiation) over a few weeks. Some might have rebounds higher than baseline.

- According to the U.S. Department of Health and Human Services, viral rebound has been observed as early as 3 to 6 days after stopping treatment.[6]
- In a person with a previously supressed viral load, HIV becomes detectable in the blood within 7–14 days of interrupting treatment (Li et al., 2015, Nature)
- In the AIDS Clinical Trials Group study (ACTG) A5345 where ART was interrupted in a closely monitored clinical trial setting, it took a median of 22 days to a rebound above 1000 copies per ml.[7]
- In a WHO policy brief on: The Role of HIV Viral Suppression in Improving Individual Health and Reducing Transmission[8], three key categories of viral load were defined: **unsuppressed** (above 1000 copies/mL), suppressed (detected but less than 1000 copies/mL), and undetectable (not detected by the test or sample type used). Detectable Viral load can count at a level of less than 1000 copies/mL indicate that some virus is replicating and present, and could be due to missing doses, recent treatment initiation or drug resistance.

How quickly do people become infectious after stopping ART?

After discontinuing ART, individuals with previously suppressed HIV can experience a rapid increase in viral load, often reaching detectable levels within **days to weeks**. This viral load rebound elevates the risk of HIV transmission, rendering individuals infectious shortly after stopping ART.[9] The higher the viral load, the higher the infectiousness, particularly in sexual and vertical transmission (transmission from mother to child during pregnancy or through breastfeeding).

- *Vertical transmission of HIV*
  Interrupting antiretroviral therapy during pregnancy significantly increases the risk of perinatal HIV transmission, especially in the third trimester.
  - ART interruption in the third trimester was associated with a transmission rate of 18.2%, compared to 1.3% in the overall cohort.[10]

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1 2024 GLOBAL AIDS UPDATE Thematic briefing note. People Living with HIV. Available at URL: https://www.unaids.org/sites/default/files/media_asset/2024-unaids-global-aids-update-living-with-hiv_en.pdf

2 https://www.unaids.org/en/impact-US-funding-cuts

3 https://www.who.int/news-room/questions-and-answers/item/guidance-on-handling-interruptions-in-antiretroviral-treatment-due-to-hiv-service-disruptions--drug-shortages--or-stockouts

4 2024 GLOBAL AIDS UPDATE Thematic briefing note. People Living with HIV. Available at URL: People living with HIV—Thematic briefing note—2024 global AIDS update The Urgency of Now: AIDS at a Crossroads

5 Nature. 1995 Jan 12;373(6510):117-22. doi: 10.1038/373117a0. Abstract access: Viral dynamics in human immunodeficiency virus type 1 infection—PubMed

6 Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Available at URL: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/arv-therapy-as-prevention

7 Jonathan Z Li, Evgenia Aga, Ronald J Bosch, et al. AIDS Clinical Trials Group A5345 Study Team, Time to Viral Rebound After Interruption of Modern Antiretroviral Therapies, *Clinical Infectious Diseases*, Volume 74, Issue 5, 1 March 2022, Pages 865–870. Available at URL: https://doi.org/10.1093/cid/ciab541

8 https://www.who.int/publications/i/item/9789240055179

9 Gunst, J.D., Gohil, J., Li, J.Z. et al. Time to HIV viral rebound and frequency of post-treatment control after analytical interruption of antiretroviral therapy: an individual data-based meta-analysis of 24 prospective studies. *Nat Commun* 16, 906 (2025). Available at URL: https://doi.org/10.1038/s41467-025-56116-1

10 Galli L, Puliti D, Chiappini E, et al. Is the interruption of antiretroviral treatment during pregnancy an additional major risk factor for mother-to-child transmission of HIV type 1? *Clin Infect Dis.* 2009;48(9):1310-1317. Available at: https://pubmed.ncbi.nlm.nih.gov/19309307.

- The risk of perinatal HIV transmission is very high at maternal viral load levels above 1000 copies/mL before delivery (Drake et al., 2014, JAIDS).
- Interrupting ART during breastfeeding can lead to increased viral load in mothers, thereby elevating the risk of vertical transmission. A systematic review and meta-analysis found that among breastfed infants whose mothers received ART, the overall pooled transmission rates were 3.54% at 6 months and 4.23% at 12 months. However, transmission risk increased once ART was stopped at six months postpartum, underscoring the importance of continuous ART during breastfeeding[11]

- *Treatment among children*
  Interruptions in HIV treatment have been associated with higher mortality among children living with HIV. Children living with HIV experienced notable rates of interruptions in HIV treatment and mortality, with children living with HIV under 5 years old experiencing a disproportionate share of these outcomes, underscoring the importance of targeted interventions such as early diagnosis of HIV and differentiated service delivery models that support rapid ART initiation and retention in care.[12]
- *HIV transmission through injection drug use*
  Interruptions in ART among people who inject drugs can lead to increased community HIV transmission. A study examining ART interruptions among HIV-positive individuals who use drugs highlighted that such interruptions undermine the effectiveness of treatment as prevention strategies, potentially elevating the risk of onward HIV transmission.[13]
  - Higher viral loads increase the likelihood of HIV transmission via shared needles.
  - ART interruption among people who inject drugs has been linked to higher community HIV spread (Stopka et al., 2019).

How fast could the HIV virus become resistant to drugs when treatment is interrupted?

Genetic mutations are an inevitable consequence of any HIV replication—because HIV replication is a very rapid and error-prone process. Exposure to ARVs slows down virus replication but also encourages development of resistance mutations. This is particularly the case if there is ongoing viral replication in the presence of sub-optimal drug levels, such as when drug doses are missed, when a patient takes only 1-2 components of a full combination regimen or takes lower doses, as may happen during stock outs or interruption of services, resistance to ARVs will develop.

Drug resistance after stopping ART can develop within several weeks, particularly since some drugs in a combination regimen remain in the body longer than others, creating a situation where HIV is exposed to only one or two drugs instead of to a full suppressive regimen.

Resistance development differs with and between ARV drug classes for example:

- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) like Efavirenz, Nevirapine and Rilpivirine have a long half-life, meaning they remain in the body longer. Resistance to NNRTIs can develop within a few weeks due to their long half-life and low genetic barriers (Nijhuis et al., 2009).
- Nucleoside Reverse Transcriptase Inhibitor (NRTIs) (e.g., Tenofovir, Lamivudine, Zidovudine): Resistance occurs more slowly but can still emerge within several weeks if ART is interrupted repeatedly.
- Protease Inhibitors (PIs) (e.g. Darunavir/ritonavir, Lopinavir/ritonavir) & Integrase Strand Transfer Inhibitors (INSTIs) (e.g., Dolutegravir): These drugs have a higher barrier to resistance, but resistance can develop if ART is stopped and restarted inconsistently.

Resistance to ARVs can compromise the available treatment options for people living with HIV, especially due to long-term persistence of achieved mutations in HIV latently infected cells. This could be particularly problematic in resource-limited settings.

What are the clinical consequences when people's immune function has declined?

CD4+ cell count is the main clinical measure of immune function and an accepted predictor of risk of HIV related infectious diseases. Clinicians usually tell patients that a "normal" CD4+ is between 500 and 1500 cells/mm³ and indicates a strong immune system.

Interrupting ART in individuals with HIV can lead to rapid viral load rebound, resulting in a decline in CD4+ T-cell counts and increased susceptibility to opportunistic infections (OIs). The extent and rate of immune system decline vary among individuals, influenced by factors such as baseline CD4+ counts and the duration of ART interruption.

Patients who have been on long term treatment could experience a decline of up to 100 CD4+ cells/mm³ within a few weeks after stopping treatment. Serious clinical consequences / risk of illness are linked to reduced CD4+ cell counts after interrupting treatment.

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[11] Maganizo B Chagomerana, Timing of HIV testing among pregnant and breastfeeding women and risk of mother-to-child HIV transmission in Malawi: a sampling-based cohort study, https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25687?utm_source=chatgpt.com

[12] https://www.croiconference.org/abstract/3515-2025/

[13] McNeil, R., Kerr, T., Coleman, B. *et al.* Antiretroviral Therapy Interruption Among HIV Postive People Who Use Drugs in a Setting with a Community-Wide HIV Treatment-as-Prevention Initiative. *AIDS Behav* 21, 402–409 (2017). Available at URL : https://link.springer.com/article/10.1007/s10461-016-1470-2

- TB risk is higher in people with HIV and this risk is present at any CD4+ cell count.
- At CD4+ below 350 cells/mm³, bacterial pneumonia, diarrheal infections and skin problems become more frequent.
- As CD4+ drop below 200 cells/mm³, the more disabling severe opportunistic infections of AIDS kick in e.g. Pneumocystis Pneumonia (PCP), Central Nervous System toxoplasmosis, cryptococcal meningitis, or the Cytomegalovirus infection of the retina that can cause blindness.

These infectious complications are not only disabling and often fatal but place an immediate and increased strain on health care system resources in every country.

Impact of treatment interruption on prevention of HIV transmission

Scientific evidence has shown ART can reduce the probability of HIV transmission through sexual contact and during pregnancy and breastfeeding periods. In fact, a person living with HIV who is on ART who has an undetectable viral load cannot pass HIV sexually to their partners. This is often referred to as Undetectable = Untransmittable (U = U)[14]. For a person with a suppressed viral load (viral load < 1000 copies / mL), the risk of transmitting HIV to a sexual partner is almost zero or negligible, while pregnant or breastfeeding women with an undetectable viral load have minimal risk of transmitting HIV vertically to their children. However, the **U=U concept only works when people are taking ART and have undetected HIV viral load**. When the treatment is interrupted, all these benefits—referred to as Treatment as Prevention, will diminish or be jeopardised. This will lead to additional new HIV infections, increasing the number of people who will need life-long treatment and in turn increasing the global resources needed for the HIV response.

What is UNAIDS and WHO doing to prevent ART interruption and mitigate its impact?

UNAIDS and WHO are advocating for uninterrupted life-saving medication and supportive services with donors, government stakeholders and other partners. With close collaboration, UNAIDS and WHO, are engaging with communities, governments and donors to:

- Provide support to collect and analyze the real-time information and data on service interruption and utilize this information to advocate for greater solidarity on continued access to life-saving HIV treatment.
- Minimize Lost-to-Follow Up (LTFU). As treatment interruption leads to viral load rebound, identifying those likely to be LTFU and re-engaging them into care as soon as possible is a key programmatic area. Differentiated service delivery (DSD) approaches, good connection between facility-based and community-based services with the support from a functional health system is crucial. These are among the critical functions of community peer support groups and drop-in-centers for key and vulnerable populations.
- WHO is working on providing guidance on mitigation of the impact of ART interruption for programmes and networks of people living with HIV, including a public Q&A as mentioned earlier.
- There is additional information that people living with HIV and community groups may find useful in mitigating the impact of ART interruptions in the fact sheet produced by HIV i-Base, an HIV treatment activist organization[15].
- In the mid-to-longer term, all efforts need to be made to strengthen country-owned and adapted systems for health that deliver people-centred, sustainable HIV services and to prioritize diversified financing mechanisms.

[14] Undetectable = untransmittable — Public health and HIV viral load suppression | UNAIDS

[15] https://i-base.info/qa/25879#what-if-I-am-running-out-of-meds

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