



### Was higher viral load responsible for the African HIV epidemic?

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Researchers from Cornell University in New York have found that the average HIV viral load of people not taking antiretroviral medication (ART) in Africa, and especially in southern and eastern Africa, is higher than the viral loads of untreated patients in other parts of the world. The so-called 'community viral load' (CVL) off treatment was nearly four times higher on average in sub-Saharan Africa as a whole, and 5.5 times higher in southern African countries excluding South Africa, than it was in North America.

The researchers used a mathematical model to estimate that 1 in 7 HIV infections in sub-Saharan Africa would not have happened if the CVL in untreated people had been the same as in richer regions. Their model found that this effect was especially marked in low-risk populations such as heterosexual people with few partners.

#### Off-treatment viral load is higher in Africa

The observed CVLs were gathered from a number of cohort studies of people with HIV who were not on ART in various parts of the world. Viral loads from over 66 000 people in 39 different cohort groups were gathered and divided into four CD4 count ranges (under 200, 200 - 350, 350 - 500, and over 500 cells/mm<sup>3</sup>). There was a big geographical imbalance, with nearly half of all samples from Europe and under 400,

from a single cohort study, from South America, limiting the precision of the CVL estimate from this region.

Average viral loads off treatment were actually quite similar around the world. They were lower in people with the highest CD4 counts, where they ranged from approximately 5 000 in the USA to 15 000 in east Africa (3.65 - 4.18 logs), and highest in people with the lowest CD4 counts, ranging from 15 000 in South America to 220 000 in west Africa (4.17 - 5.33 logs).

Viral loads in west, east and southern Africa were consistently higher than viral loads elsewhere. The CVL was also significantly, but modestly, higher in Asia (about 40% or 0.14 logs higher). South Africa was considered separately because of its relatively better health system than other countries in the area; there, the average viral load was about 50% or 1.9 logs higher than in North America.

#### Implications for HIV infection

Putting these viral load data into a model using previous findings on the degree to which rising viral load increases infectiousness, and using population data from the epidemic in Kisumu, Kenya, the researchers calculated that by 2010 cumulative HIV prevalence in an untreated population would be 14.4% greater if untreated CVL was at the level seen in Africa rather than in North America; in other words, 1 in 7 HIV infections was directly attributable to the higher viral load.

However, raised viral load also skews demographics because it disproportionately affects people at lower risk of HIV (because people at higher risk would become infected even if CVL was lower, due to greater frequency of unprotected sex). This means that HIV prevalence in lower-risk heterosexuals was 22.5% higher than it otherwise would have been; nearly 1 in 4 infections in this group was directly attributable to higher CVL.

The researchers also calculated that a 34% decline in the frequency of sex (or a 51% increase in protected sex) would be needed to compensate for the viral load effect seen. Their model showed that the effect of higher CVL would be particularly marked at the

mid-point of the epidemic's growth. Using an assumption that HIV prevalence first started to rise significantly in 1980, they found that, with the observed CVL, the steepest point in the epidemic's growth occurred at about 1988. If CVL had been the global average in Africa, this point would not have been reached until 7 years later, leading to a modelled HIV prevalence of about 20% in the mid-90s rather than 8% - pretty close to what actually happened in southern Africa.

#### Questions and conclusions

What is causing the excess viral load? The researchers speculate that the higher rate of untreated co-infections in Africa could be to blame, and cite a 2002 paper from Uganda that shows that a herpes attack can raise HIV viral load by 50%, active tuberculosis by 150%, and acute malaria by 370% (a nearly fivefold increase).

This fact has been known for some time, and although trials that attempt to reduce HIV incidence by treating other diseases such as herpes and inflammatory STIs have tended to produce negative results, the concept is not dead; a trial in Kenya is currently looking at the effect on HIV of treating worm infestations.

This study shows that raised viral load cannot be the entire explanation for south and east Africa's dramatically larger HIV epidemics: a combination of factors ranging from it being HIV's home continent to war and poverty contributed to its unique spread into the general population.

It does, however, show that higher viral load probably made a very significant contribution at a key point in the epidemic in Africa and underlines, as the researchers say, the idea that controlling HIV viral load with antiretrovirals is key to stopping further infection. It also suggests that, until universal ART coverage is achieved, treating co-infections with the right cheaper therapies 'may offer a complementary strategy for the control of HIV in sub-Saharan Africa.'

Abu-Raddad LJ, et al. Have the explosive HIV epidemics in sub-Saharan Africa been driven by higher community viral load? *AIDS* 24, early online edition. [<http://dx.doi.org/10.1097/QAD.0b013e32835cb927.2013>]

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