



# Peer Community In Evolutionary Biology

## Predicting HIV virulence evolution in response to widespread treatment

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Herbeck JT, Mittler JE, Gottlieb GS, Goodreau SM, Murphy JT, Cori A, Pickles M, Fraser C (2016) Evolution of HIV virulence in response to widespread scale up of antiretroviral therapy: a modeling study. bioRxiv, ver. 1, peer-reviewed and recommended by Peer Community in Evolutionary Biology. <https://doi.org/10.1093/ve/vew028>

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It is a classical result in the virulence evolution literature that treatments decreasing parasite replication within the host should select for higher replication rates, thus driving increased levels of virulence if the two are correlated. There is some evidence for this in vitro but very little in the field. HIV infections in humans offer a unique opportunity to go beyond the simple predictions that treatments should favour more virulent strains because many details of this host-parasite system are known, especially the link between set-point virus load, transmission rate and virulence. To tackle this question, Herbeck *et al.*\* [1] used a detailed individual-based model. This is original because it allows them to integrate existing knowledge from the epidemiology and evolution of HIV (e.g. recent estimates of the 'heritability' of set-point virus load from one infection to the next). This detailed model allows them to formulate predictions regarding the effect of different treatment policies; especially regarding the current policy switch away from treatment initiation based on CD4 counts towards universal treatment. The results show that, perhaps as expected from the theory, treatments based on the level of remaining host target cells (CD4 T cells) do not affect virulence evolution because they do not strongly affect the virulence level that maximizes HIV's transmission potential. However, early treatments can lead to moderate increase in virulence within several years if coverage is high enough. These results seem quite robust to variation of all the parameters in realistic ranges. The great step forward in this model is the ability to obtain quantitative prediction regarding how a virus may evolve in response to public health policies. Here the main conclusion is that given our current knowledge in HIV biology, the risk of virulence evolution is perhaps more limited than expected from a direct application of virulence evolution model. Interestingly, the authors also conclude that recently observed increased in HIV virulence [2-3] cannot be explained by the impact of antiretroviral therapy alone; which raises the question about the main mechanism behind this increase. Finally, the authors make the interesting suggestion that "changing virulence is amenable to being monitored

alongside transmitted drug resistance in sentinel surveillance”.

**References:**

- [1] Herbeck JT, Mittler JE, Gottlieb GS, Goodreau SM, Murphy JT, Cori A, Pickles M, Fraser C. 2016. Evolution of HIV virulence in response to widespread scale up of antiretroviral therapy: a modeling study. *Virus Evolution* 2:vew028. doi: [10.1093/ve/vew028](<https://doi.org/10.1093/ve/vew028>)
- [2] Herbeck JT, Müller V, Maust BS, Ledergerber B, Torti C, et al. 2012. Is the virulence of HIV changing? A meta-analysis of trends in prognostic markers of HIV disease progression and transmission. *AIDS* 26:193-205. doi: [10.1097/QAD.0b013e32834db418](<https://doi.org/10.1097/QAD.0b013e32834db418>)
- [3] Pantazis N, Porter K, Costagliola D, De Luca A, Ghosn J, et al. 2014. Temporal trends in prognostic markers of HIV-1 virulence and transmissibility: an observational cohort study. *Lancet HIV* 1:e119-26. doi: [10.1016/s2352-3018(14)00002-2]([https://doi.org/10.1016/s2352-3018\(14\)00002-2](https://doi.org/10.1016/s2352-3018(14)00002-2))

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