

Timing of therapy initiation

PE55

**Initiation of Antiretroviral Therapy at high CD4 cell counts is associated with Increased Adherence, Viral Suppression, and Decreased HIV Drug Resistance in British Columbia, Canada.**

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**Background:** Early initiation of combined antiretroviral therapy (cART) has been shown to have a consistent beneficial impact on morbidity and mortality. Conversely, there is limited research investigating the possible mechanisms of how starting cART at higher CD4s decreases mortality. Therefore, we conducted this present study to investigate the association between initiating cART at different CD4 cutoffs with: short- and long-term achievement of viral suppression; the emergence of drug resistance and of an AIDS-defining illness (ADI); long-term treatment adherence; and all-cause mortality.

**Methods:** This retrospective cohort study included 4120 antiretroviral naïve patients who initiated cART between 2000 and 2012. Patients were followed until 2013, death or until the last contact date (varied by outcome). The main exposure variable included the interaction between the period of cART initiation (2000-2006 and 2007-2012) and CD4 at cART initiation categorized as < 500 versus ≥500 cells/mm<sup>3</sup>. We considered both baseline and longitudinal covariates. We fitted different multivariable models using cross-sectional and longitudinal statistical methods, depending on the outcome.

**Results:** Initiation of cART at CD4s ≥500 cells/mm<sup>3</sup> was associated with several positive treatment outcomes, suggesting that these outcomes are likely to play an important role in explaining the positive impact of early cART initiation on mortality. Patients who initiated cART with a CD4 ≥500 cells/mm<sup>3</sup> in 2007-2012 had an increased likelihood of achieving viral suppression at nine months and of maintaining an adherence level ≥95% over time, and the lowest probability of developing any resistance and an ADI during follow-up. Patients who initiated cART with a CD4 ≥500 cells/mm<sup>3</sup> in 2007-2012 were not the ones with the highest likelihood of maintaining viral suppression over time, most likely due to viral load blips that have happened during the follow-up time. Despite these viral load blips resulting in a perceived lower probability of maintaining viral suppression over time, we showed that this outcome did not negatively influence the mortality of these patients.

Variable	Cross-sectional Analysis			Longitudinal Analysis		
	Predicted probability of achieving viral suppression in nine months	Predicted probability of maintaining adherence ≥95% over time	Predicted probability of maintaining viral suppression over time	Predicted probability of developing resistance to any drug class over time	Predicted probability of developing an AIDS-defining illness by the end of follow-up	Predicted probability of being dead by the end of follow-up
Period & CD4 cell count (cells/mm <sup>3</sup> ), median (Q1-Q3)						
2000-2006 & <500	0.78 (0.60 - 0.81)	0.75 (0.63 - 0.84)	0.77 (0.58 - 0.90)	0.11 (0.07 - 0.18)	0.04 (0.02 - 0.08)	0.13 (0.06 - 0.22)
2000-2006 & ≥500	0.70 (0.40 - 0.82)	0.55 (0.36 - 0.70)	0.51 (0.23 - 0.79)	0.04 (0.01 - 0.08)	0.02 (0.01 - 0.03)	0.16 (0.10 - 0.24)
2007-2012 & <500	0.82 (0.65 - 0.87)	0.82 (0.73 - 0.87)	0.68 (0.58 - 0.78)	0.04 (0.03 - 0.07)	0.03 (0.02 - 0.04)	0.05 (0.03 - 0.08)
2007-2012 & ≥500	0.90 (0.85 - 0.94)	0.84 (0.75 - 0.88)	0.63 (0.55 - 0.74)	0.01 (0.01 - 0.02)	0.01 (0.00 - 0.02)	0.03 (0.01 - 0.03)

Footnote: Q1: 25<sup>th</sup> percentile, Q3: 75<sup>th</sup> percentile

[Predicted Probabilities - Multivariable Models]

**Conclusions:** Our results should alleviate some of the concerns clinicians may have when initiating cART in people with CD4s ≥500 cells/mm<sup>3</sup>, as recommended by current guidelines, particularly where free access to modern cART and related monitoring is available.