

# Predictors of CD4:CD8 Ratio Normalization and its Effect on Health Outcomes in the Era of Combination Antiretroviral Therapy

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## Objective

This study investigated the incidence and clinical predictors of CD4:CD8 ratio normalization following the initiation of combination antiretroviral therapy (cART). This study also examined whether CD4:CD8 ratio can serve as a prognostic marker for improved HIV-related health outcomes.

## Main Findings

- Few HIV-positive patients normalized their CD4:CD8 ratios within the first few years of initiating cART.
- The CD4:CD8 ratio provided no additional short-term predictive value after accounting for other risk factors.

## Background

- HIV infection is accompanied by a spike in CD8+ T-cells, which results in an inverted CD4:CD8 ratio.
- Even though the CD4+ T-cell count increases following successful cART, the CD4:CD8 ratio often remains inverted and fails to normalize. The reasons for this are unclear.

## Importance of this Study

- While CD4+ T-cell count has long served as a prognostic marker for HIV/AIDS outcomes, recent attention has focused on immune activation as an independent predictor of future clinical events and mortality.
- This study examines the potential role of the CD4:CD8 ratio as an indicator of immune status and immune recovery.
- This is the first study to describe CD4:CD8 ratio normalization within a large cohort of cART treated patients.

## How this Study was Conducted

- Data were analyzed from the CANOC collaboration, an interprovincial collaborative cohort of HIV-positive individuals on antiretroviral therapy in Canada.
- CANOC compiled HIV clinical, virological, immunologic, and demographic data from 8 cohorts across British Columbia, Ontario, Quebec.
- 4,206 participants from the CANOC collaboration were included in this analysis.
- The median follow-up duration was 2.77 years
- Normalization was defined as a CD4:CD8 ratio greater than or equal to 1.2.

## Study Results

- Only 7.2% of participants achieved a normal CD4:CD8 ratio during the study period.
- Factors that were significantly associated with achieving a normal CD4:CD8 ratio were: higher baseline CD4+ T-cell count, lower baseline CD8+ T-cell count, time-updated HIV RNA suppression, and not reporting sex with other men.
- Achieving a normal CD4:CD8 ratio was not associated with time to AIDS defining illness/death.

## Implications

- The fact that so few patients achieved normal CD4:CD8 ratios suggests that the vast majority of successfully treated HIV-positive patients remain immunologically impaired.
- Future studies should determine if the CD4:CD8 ratio is relevant to non-AIDS outcomes such as risk for cardiovascular disease and cancer.

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