

# CD4/CD8 Ratio and Cancer Risk among Adults with HIV

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## Abstract

**Background:** Independent of CD4 cell count, low CD4/CD8 ratio in people with HIV (PWH) is associated with deleterious immune senescence, activation, and inflammation, which may contribute to carcinogenesis and excess cancer risk. We examined whether low CD4/CD8 ratios predicted cancer among PWH in the USA and Canada.

**Methods:** We examined all cancer-free PWH with one or more CD4/CD8 values from NA-ACCORD observational cohorts with validated cancer diagnoses between 1998-2016. We evaluated the association between time-lagged CD4/CD8 ratio and risk of specific cancers in multivariable, time-updated Cox proportional hazard models using restricted cubic splines. Models were adjusted for age, sex, race and ethnicity, hepatitis C virus, and time-updated CD4 cell count, HIV RNA, and history of AIDS-defining illness.

**Results:** Among 83,893 PWH, there were 5,628 incident cancers, including lung cancer (n = 755), Kaposi sarcoma (KS, n = 501), non-Hodgkin lymphoma (NHL, n = 497), and anal cancer (n = 439). Median age at cohort entry was 43 years. Overall median six-month lagged CD4/CD8 ratio was 0.52 (interquartile range: 0.30-0.82). Compared with a six-month lagged CD4/CD8 of 0.80, a CD4/CD8 of 0.30 was associated with increased risk of any incident cancer (adjusted hazard ratio = 1.24 [95%CI: 1.14-1.35]). CD4/CD8 ratio was also inversely associated with NHL, KS, lung cancer, anal cancer, and colorectal cancer in adjusted analyses (all 2-sided p < 0.05). Results were similar using 12-, 18-, and 24-month lagged CD4/CD8 values.

**Conclusions:** Low CD4/CD8 ratio up to 24 months prior to cancer diagnosis was independently associated with increased cancer risk in PWH and may serve as a clinical biomarker.

**Keywords:** CD4/CD8; HIV; anal cancer; cancer; lung cancer.