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Elite controllers in a cohort of people with well-estimated dates of HIV seroconversion: characteristics, time to lose elite status and natural CD4 evolution

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PURPOSE

- **Background**: Elite controllers (EC) are a minority of people with HIV who maintain low or undetectable viraemia without ART. However, elite control is usually not permanent.
- **Purpose**: The objectives were to explore factors associated with EC, to estimate the time to loss of EC status and related factors, and to examine CD4 cell count evolution in EC and non-EC during the natural history of infection.

METHODS

- Data source: CASCADE Collaboration - Multinational study of cohorts of HIV seroconverters (individuals with HIV-1 test window ≤12 months or other laboratory evidence of seroconversion)
- Eligibility: ≥ 16 years old at HIV diagnosis and with ≥1 viral load (VL) measurement pre-ART
- Elite Controller: ≥3 undetectable VL measurements while ART-naïve (span ≥1 year) without previous VL>1000 copies/mL
- Loss of EC status: 2 consecutive detectable VL (virologic rebound) or ART initiation
- Statistical analysis: logistic regression (factors associated with EC), time-to-event methods including competing risks analysis (loss of EC; virologic rebound and ART initiation as competing events), mixed models with natural cubic splines (CD4 evolution)

CONCLUSIONS

- EC was rare (0.65%; 95% CI: 0.56% – 0.75%) but more frequent in those who acquired HIV through heterosexual contact and those of African origin
- By 3 years after EC, 30% had experienced virologic rebound and 19% had started ART with an undetectable viral load
- Understanding mechanisms of viraemic control in Elite Controllers could facilitate development of therapeutic vaccines and functional cure

RESULTS

- Among 35,729 individuals, 27,819 were eligible (median age 32; 85% men; 71% MSM; 80% European/N. American, median seroconversion year: 2008). Of these:
  - **180 (0.65%; 95% CI: 0.56% – 0.75%) were elite controllers**
  - 27,200 (97.77%; 95% CI: 97.59% – 97.94%) were not elite controllers
  - 439 (1.58%; 95% CI: 1.43% – 1.73%) were of undetermined status and excluded from subsequent analyses.
- Elite control was:
  - more frequent in men who acquired HIV through heterosexual contact (HET) (aOR 1.80; 95%CI: 1.11-2.93), HET women (1.96; 1.30-2.98) and people who inject drugs (1.62; 0.96-2.74) compared to MSM, and similarly in those from sub-Saharan African countries (1.80; 1.11-2.90 compared to those from Europe/N. America)
  - less frequent in those diagnosed during acute infection (0.70; 0.51-0.95)
- Median (95% CI) time to elite control loss (due to virologic rebound or ART initiation) was 3.31 (2.16, 4.33) years
  - 77 (42.8%) EC progressed to virological rebound while off ART
  - 39 (21.7%) initiated ART while their viral load was undetectable (**Figure 1)**
- EC loss due to virological rebound was less frequent with increasing age (aHR: 0.73; 0.55-0.96 per 10 years) and in people who inject drugs and HET women (0.32; 0.13-0.80 and 0.50; 0.24-1.02 compared to MSM, respectively)
- Initial CD4 count was higher for elite controllers, with a prolonged period of increasing CD4 followed by a slow decrease (**Figure 2**)

Figure 1. *Loss of EC status due to detectable VL or ART initiation - Competing risks analysis*

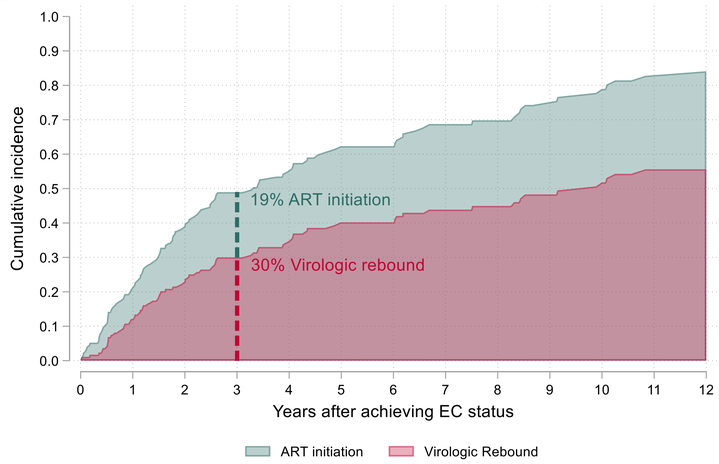
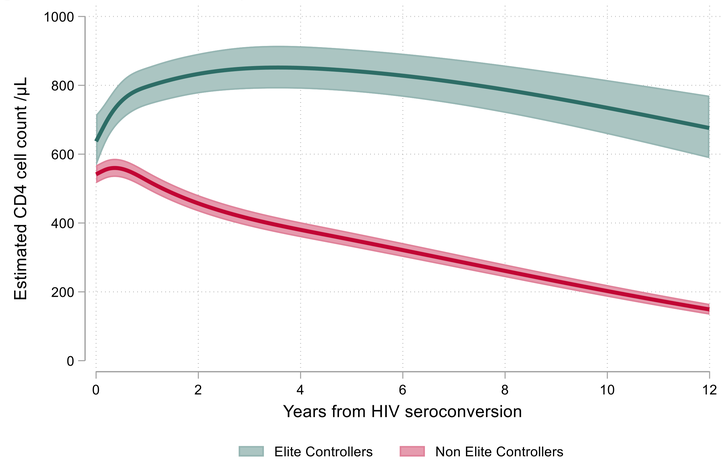


Figure 2. *CD4 cell count evolution pre-ART/AIDS in Elite Controllers and non-Elite Controllers*



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https://www.ucl.ac.uk/population-health-sciences/cascade-study