

# Long term non-progressors and elite controllers: starting antiretroviral therapy in routine HIV care

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## Introduction

There is now good evidence<sup>1,2</sup> for starting antiretroviral therapy (ART) in HIV-positive individuals regardless of CD4 count. However, there are well-known populations who appear to possess an element of natural virological control through as-yet uncertain means<sup>3</sup>. They are usually termed long term non-progressors (LTNP) and elite controllers (EC) depending on the degree of control. Such individuals have preserved CD4 counts and low viral loads. There is little evidence or guidance regarding ART usage in these patients<sup>4</sup>, and treatment guidelines have changed to recommend ART for all, due to results from the START study and others. However, the START trial included few LTNP or EC and so this recommendation is not evidence based for these subsets. We sought to identify these patients within our HIV-positive population, and their outcomes including ART commencement and development of opportunistic infections (OI) or malignancy.

## Method

We identified those defined by clinicians as LTNP/EC by searching clinical records from 2000-2015 for "progressor" or "elite", in a regional centre providing care for around 2600 HIV-positive individuals.

Definitions used for both subsets were as shown in Table 1<sup>4</sup>. Medical staff used a proforma to collect data including demographics, disease progression, ART use and the reasons for this. Descriptive analysis was performed using Excel and STATA.

Exclusions included any patient who had not maintained LTNP status for at least 7 years, and those lost to follow-up by leaving the area as we were unable to determine if they fulfilled this criteria.

Long term non-progressor	Elite Controller
CD4 > 500 cell/ml (majority readings)	Any CD4 count
VL < 10000 copies/ml	VL < 40 copies/ml
No OIs	No OIs
No ART (except PMTCT prophylaxis)	No ART
Duration ≥ 7 years	Two VL readings over 12 months

Table 1: LTNP/EC definitions

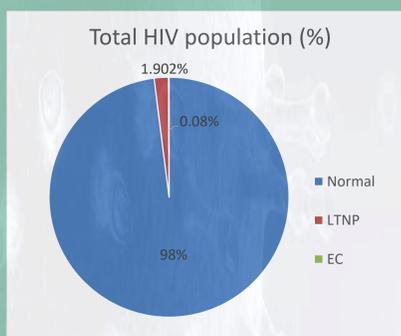


Figure 1: Percentage of LTNP/EC in HIV population

## Results

We identified 52 individuals who fit definitions for LTNP or EC in our population. The percentage of these which were LTNP/EC respectively are shown in Figure 1.

The female/male proportion was 20/52 (38%) and 32/52 (62%) respectively for LTNP, and 1/2 each for EC (50%). HIV diagnosis occurred between 1982 and 2012. Further results are shown in Table 2. Baseline and latest viral loads (VL) and CD4 counts are shown in Figure 2.

50/52 (96%) of our group were LTNP, with 2/52 (4%) EC. 34/50 (65%) LTNP started treatment during the observation period (Figure 3). 34/52 (52%) of the total population started treatment (Figure 3). The majority (27/34 (79%)) started ART due to loss of LTNP status. Other reasons included prevention of mother to child transmission (PMTCT), cardiovascular risk and development of malignancy (Figure 3). The EC by definition did not commence ART and did not lose their status in the period observed.

The number of patients who suffered an adverse outcome are shown in Table 3. OIs included pneumocystis pneumonia, TB lymphadenitis and pneumococcal pneumonia, the latter occurring on ART.

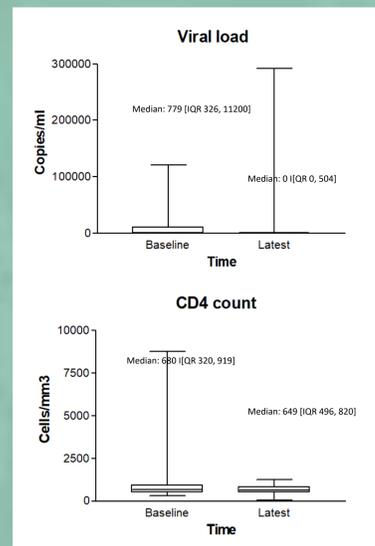


Figure 2: Baseline and latest VL/CD4 counts

	Median (years) [IQR]
Patient age	49 [23, 38]
Age at diagnosis	32 [28, 38]
LTNP status duration	10 [7, 25]
Time from diagnosis to starting ART	11 [9, 13]
Follow-up time	13 [10, 24]

Table 2: Further results

Adverse outcome	Number (%)
Opportunistic infection	10 (19)
Malignancy	4 (8)
Death	2 (4)

Table 3: Adverse outcomes

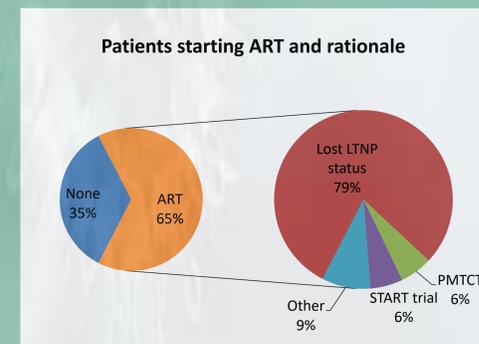


Figure 3: Patients given ART and reason for commencement (%)

## Discussion

2% (95% CI 1.4, 2.6) of our HIV population in Manchester were defined as LTNP or EC. The proportion of these patients is usually estimated at 1-5%<sup>5</sup>. Clearly, this varies by definition used, which is not standardised. Additionally we may have underestimated this due to the method used to identify patients. There is no database or record routinely kept with this information, and so we relied on manual searching and clinician recall to identify suitable patients.

Just over half of our group started on ART during observed follow up, with the vast majority losing controller status. A significant number also developed adverse outcomes such as OI, some even despite ART. This may suggest that LTNP are in fact merely slow progressors, and given enough time will all lose control similarly. In this case commencement of ART immediately as per the START trial recommendations may be appropriate, and help to reduce development of OI, etc. Alternatively this may reflect subsets within LTNP themselves outside of EC. More research is needed to clarify.

## Conclusion

- 50 LTNP and 2 EC in our group (2% of total population)
- The majority (65%) started on ART
- Loss of LTNP status was the main reason to commence ART (79%)
- Immediate ART may help prevent adverse outcomes (OI, malignancy)

## References

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