Service evaluation of current standard of care for elite controllers, viral controllers and long term non-progressors in an age of anti-retroviral therapy (ART) for all

UNIVERSITY OF LEEDS [1]

Authors: Shiwei Ooi[1], Joseph Whelan[1], Natasha Astill[2] and Harriet Wallace[2]

NHS The Leeds Teaching Hospitals NHS Trust [2]

Background:

- After initial HIV infection and viraemic spike most patients experience a continuously falling CD4 count and a continuously rising viremia, within three years most are immunocompromised (1).
- Amongst people living with HIV (PLWH) there is a small (0.4%,) but significant group of patients who's CD4 count does not drop below 500 cells/µl for many years despite the absence of Anti-retroviral Therapy (ART). These are the 'Long Term Non Progressors' (LTNPs), Fig. 1 shows this atypical progress (2,3).
- With the advancement of viral load testing, a further group of patients were defined by their ability to supress their viral load (VL) below 2000 copies/ml, they are the 'Viral Controllers' (VCs) (4).
- In the past ART would be started once CD4 count had dropped to 350 cells/µl (5).
- In 2015 a large randomised study the 'Strategic Timing of Antiretroviral Therapy (START)' was published, finding that regardless of CD4 count people who started on ART immediately were at lower risk of AIDs related and non-AIDs related illness (6,7).
- The British HIV Association (BHIVA) changed their guidelines in 2015 in line with the START study recommending that all seroconverted individuals commence ART (8).

Aims:

This study will aimed to identify the LTNP cohort receiving HIV care from Leeds teaching Hospitals NHS Trust and perform a demographic analysis. The study then performed an audit on the identified LTNPs to analyse whether they have all been offered ART as the START study recommends. The LTNPs not on ART in 2021 were isolated and reasons for not commencing ART studied. Finally, the LTNPs were separated by demographic components and disparities in rates of ART uptake were analysed.

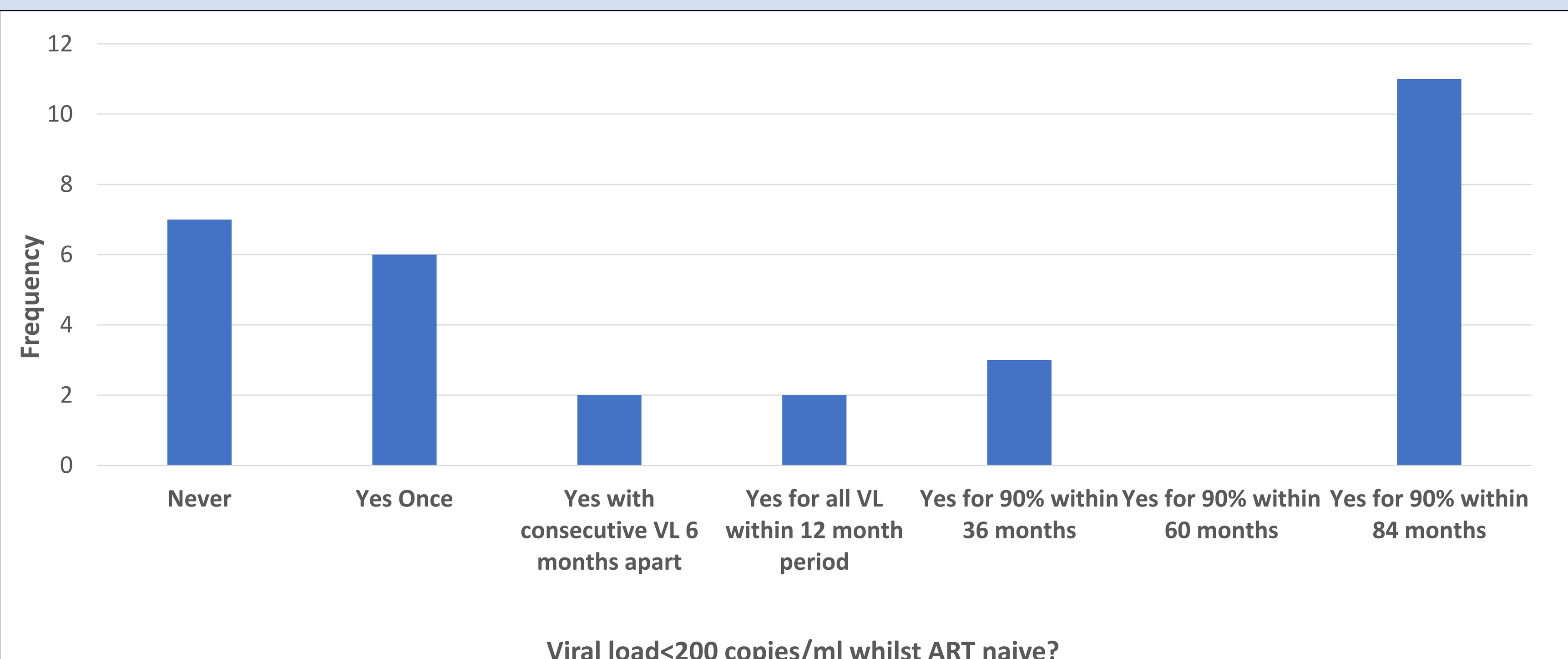

Figure 2: A bar chart showing the relative frequencies of years of VL suppression to less than 200 copies/ml* in the LTNP sample whilst ART naïve

* Viral loads recorded do not include initial seroconversion viral spike

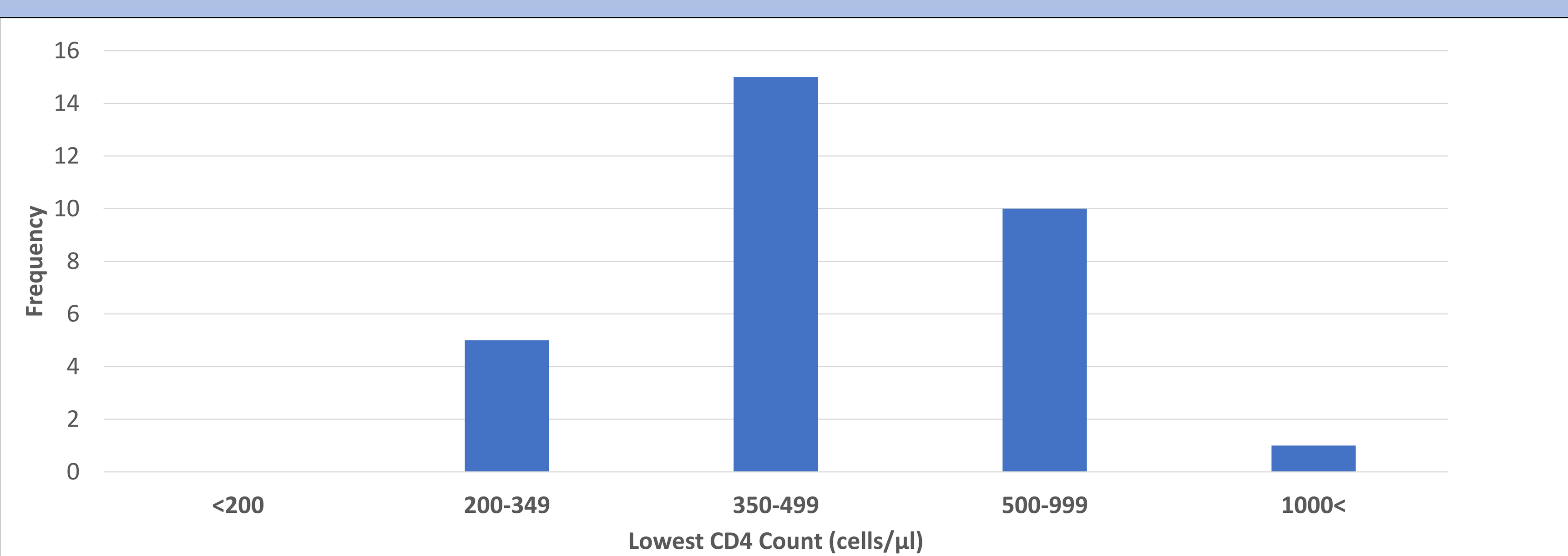

Figure 3: A bar chart showing the relative frequencies of lowest CD4 count recorded for each patient whilst ART naïve in the LTNP Sample

Conclusions:

- Amongst the Leeds PLWH are a group of 31 patients who show signs of non-progression in maintaining their CD4 count and never contracting an opportunistic infection.
- A subgroup of nine patients met the strict definition of LTNP in maintaining a CD4 count of >500 cells/ml whist ART naïve for seven years or more(3).
- Within the group of 31 LTNP all patients display some viraemic control, manging to supress VL<2000. Within these viraemic controllers there are a group of 11 Elite Controllers who supressed their viral load to an 'undetectable' level for seven years or more.
- Audit showed that all identified LTNP who were not taking ART in 2021 had had a discussion with a clinician about the change in guidance and evidence supporting ART for all, and treatment had been offered (8).
- Reasons given by LTNPs for not commencing ART were often not recorded, of those who did give a reason only one of four listed the side effects of ART.
- This work has highlighted different information needs and challenges around ART acceptance in this group of LTNP, and the importance of personalising treatment conversations.

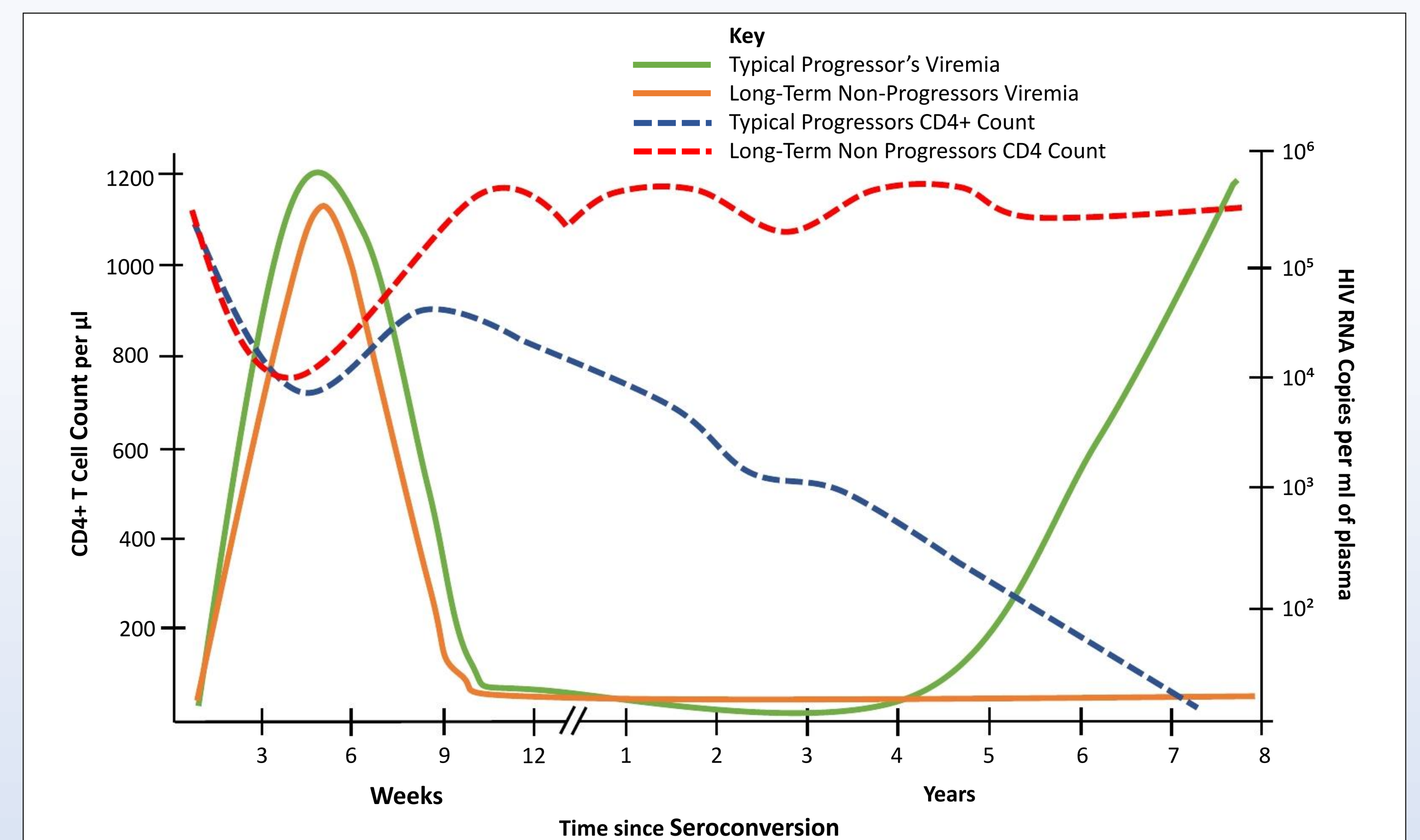

Figure 1: A graph showing typical values of CD4 count and VL in a Typical PLWH contrasting against those of a LTNP

Methods:

Identification of non-progressors LTNP was from two sources: clinician remembered cases and those identified by applying filters to the electronic patient records of PLWH in Leeds. Those identified from the records had the filters of VL<1000 and ART Naïve (never having received ART) in 2015 applied to them. Demographic analysis included crosstabulation of categorical variables and distribution of continuous statistics.

When comparing treatment offer by demographic groupings further frequency analysis was performed.

Results:

In Leeds the number of PLWH is circa 2300 patients, out of these 31 patients were identified as LTNP by clinician remembered cases and filters applied to the Electronic Patient Record. Eight of these patients were on ART for a short period of time. Further results can be seen in Fig 2,3,4 and 5. The sample was too small to correlate demographic groups with uptake of ART.

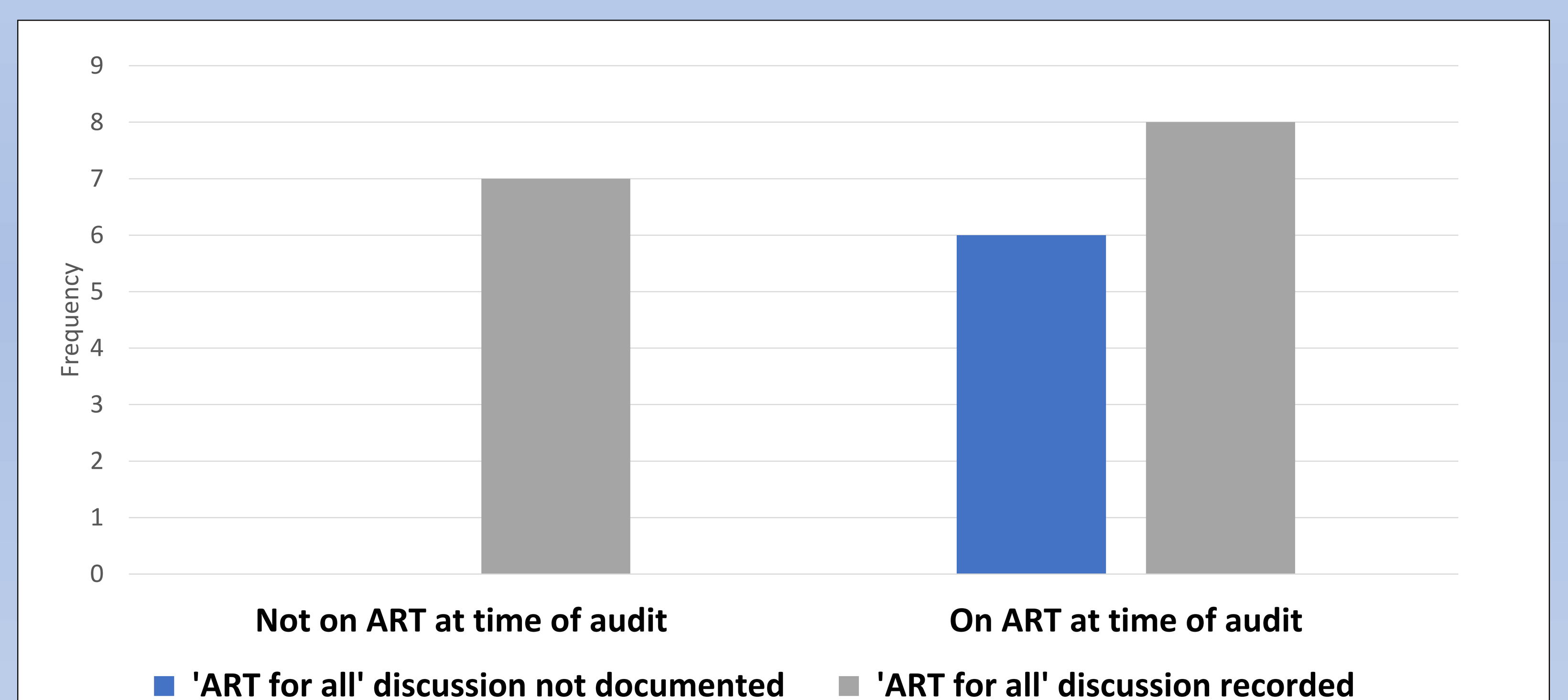

Figure 4: A Clustered Bar Chart showing ART uptake following 'ART for all' Discussion

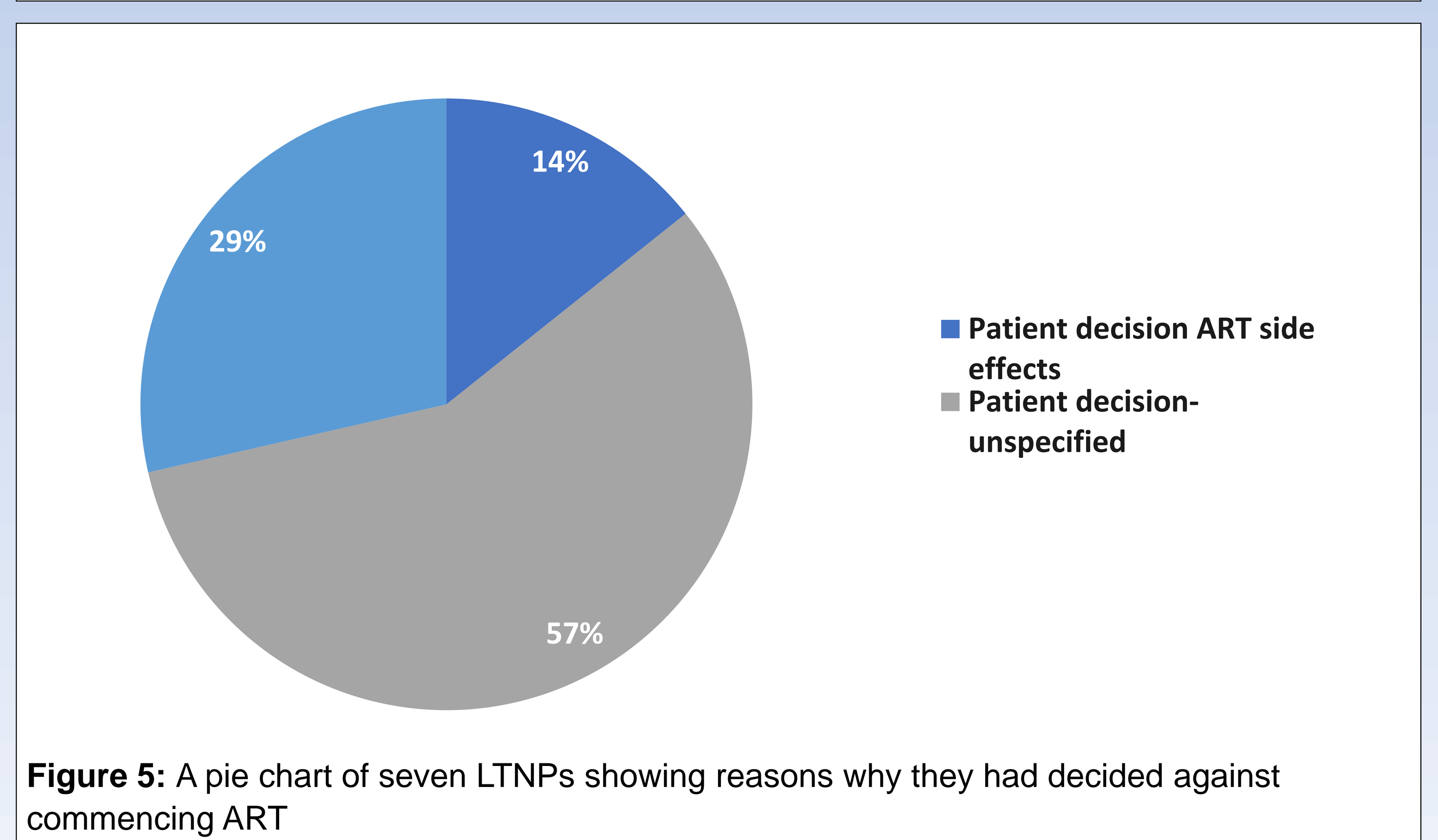

Figure 5: A pie chart of seven LTNPs showing reasons why they had decided against commencing ART

References:

1. Altfeld M, Addo MM, Rosenberg ES, Hecht FM, Lee PK, Vogel M, et al. Influence of HLA-B57 on clinical presentation and viral control during acute HIV-1 infection. AIDS. 2003;17(18).
2. Grabar S, Selinger-Leneman H, Abgrall S, Pialoux G, Weiss L, Costagliola D. Prevalence and comparative characteristics of long-term nonprogressors and HIV controller patients in the French Hospital Database on HIV. AIDS. 2009;23(9).
3. Mandalia S, Westrop SJ, Beck EJ, Nelson M, Gazzard BG, Imami N. Are Long-Term Non-Progressors Very Slow Progressors? Insights from the Chelsea and Westminster HIV Cohort, 1988–2010. PLOS ONE. 2012;7(2):e29844.
4. Deeks SG, Walker BD. Human Immunodeficiency Virus Controllers: Mechanisms of Durable Virus Control in the Absence of Antiretroviral Therapy. Immunity. 2007;27(3):406-16.
5. The Strategies for Management of Antiretroviral Therapy Study G. Major Clinical Outcomes in Antiretroviral Therapy (ART)–Naive Participants and in Those Not Receiving ART at Baseline in the SMART Study. The Journal of Infectious Diseases. 2008;197(8):1133-44.
6. The INSIGHT START Study Group. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. New England Journal of Medicine. 2015;373(9):795-807.
7. Hemkens LG, Bucher HC. HIV infection and cardiovascular disease. European Heart Journal. 2014;35(21):1373-81.
8. Churchill D, Waters L, Ahmed N, Angus B, Boffito M, Bower M, et al. BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015. 2015.