

BACKGROUND

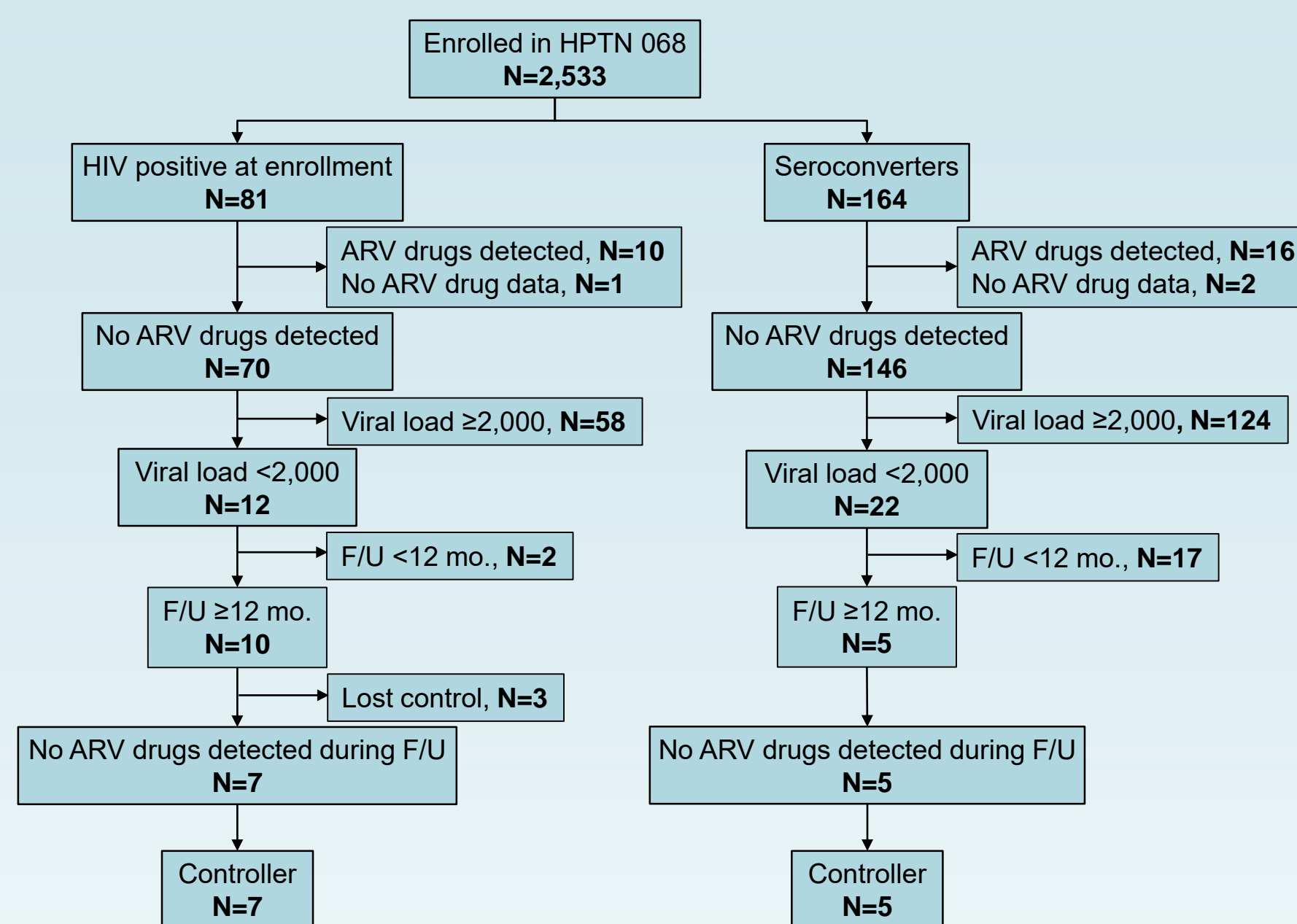
HIV controllers are able to suppress viral replication to low or undetectable levels without antiretroviral therapy (ART). Natural control of HIV infection is often characterized normal or slightly higher CD4 cell counts, normal levels of immune activity, and slower progression to AIDS. The degree of viral suppression and duration of viremic control are often used to classify individuals as viremic or elite controllers.

Differences in viral genetics, host genetics, or innate, humoral, or adaptive immune responses have been associated with natural control of HIV infection.

The HIV Prevention Trials Network (HPTN) 068 study was conducted in a rural area in South Africa and evaluated the impact on HIV incidence of a cash transfer conditional on high school attendance. The study enrolled 81 HIV-infected and 2,448 HIV-uninfected young women who were followed annually until their expected graduation date; some women had a post-graduation follow-up visit 1-2 years later. We evaluated the frequency of HIV controllers in this cohort.

RESULTS

Figure 1. Identification of viremic controllers.



Abbreviations: mo.: months; F/U: follow-up.

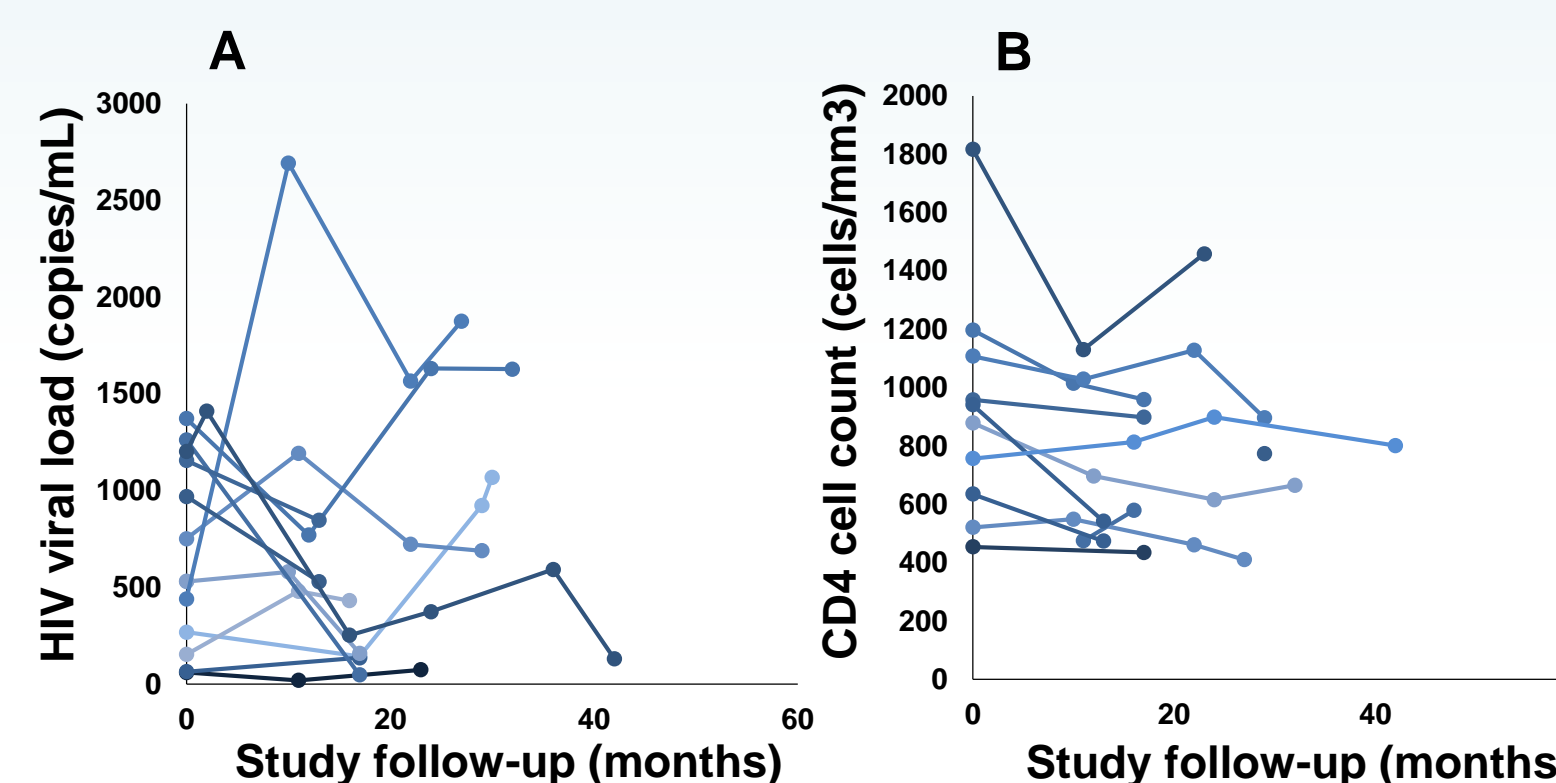
In HPTN 068, 245 women had HIV infection; 81 were HIV-infected at enrollment and 164 acquired HIV infection during the study (Figure 1). ARV drug testing was performed for 242 women. ARV drugs were detected in 26 (10.7%) women; those women were excluded from further analysis. Thirty-four (15.7%) of the remaining 216 women had a viral load <2,000 copies/mL at their first HIV-positive visit, including 3 with a viral load <40 copies/mL. The median viral load was 492 copies/mL (range: <40-1,479).

Fifteen (44.1%) of the 34 women who had an initial viral load <2,000 copies/mL were followed for at least 12 months (median follow-up period: 23 months, range: 13-51 months).

Twelve participants had sustained viral suppression (viral load <2,000 copies/mL for at least 12 months; median follow-up period: 20 months, range: 13-42; one woman had a single viral “blip” of 2,693 copies/mL during the study period; Figure 2).

None of the 12 women had a sustained viral load <40 copies/mL. ARV drugs were not detected in any samples collected during follow-up in these 12 women. These 12 women were classified as viremic controllers.

Figure 2. HIV viral load (Panel A) and CD4 cell count (Panel B) results for the 12 viremic controllers.



Viral load, age, and CD4 cell count were compared for the 12 viremic controllers and the other 204 women who had a viral load <2,000 with no ARV drugs detected at their first HIV-positive visit (Table).

Table. Characteristics of women with a viral load <2,000 and no ARV drugs detected at the first HIV-positive visit.

Parameters	Viremic controllers ^a N=12	Other women N=204	P value
First HIV-positive visit			
Median (range) viral load, copies/mL	1,063 (61-1,479)	17,911 (40-5,667,096)	NA ^b
Median (range) age, years	17.5 (16-19)	19 (13-24)	0.04
Median (range) CD4 cell count, cells/mm³	759 (448-1817)	549 (13-1440)	0.02
During follow-up			
Median (range) CD4 cell count, cells/mm³	542 (394-1130)	538 (77-1404)	0.42

^a Participants who had a HIV viral load <2,000 copies/mL at their first HIV-positive visit with sustained viral suppression for at least 12 months.

^b A p value is not reported for this comparison, since viral load was used to identify viremic controllers (NA: not applicable).

HIV genotyping results were obtained for 201 (82%) of the 245 women at their HIV-positive visit, including 5/12 viremic controllers. HIV subtyping was performed using *pol* region sequences; 200 women had subtype C infection, one had subtype A infection. All five viremic controllers had subtype C infection; the HIV drug resistance mutation, Y181C, was detected in HIV from one viremic controller.

CONCLUSIONS

- Thirty-four (15.7%) of 216 young women in this cohort from rural South Africa were virally suppressed at one or more study visits in the absence of ARV drug use.
- Sustained viral suppression was documented in 12 (80%) of 15 women who had at least one year of follow-up; those women were classified as viremic controllers.
- The duration of viral suppression could not be determined in women with <1 year of follow-up. The frequency of HIV viremic controllers in the cohort was estimated to be 12.5% [(35 x 0.8 x 100) / 216].

METHODS

STUDY COHORT

Samples were obtained from HIV-infected women aged 13-24 years who were enrolled HPTN 068 (2011-2015).

LABORATORY TESTING

The following tests were performed:

- HIV testing at enrollment and annual follow-up visits
- CD4 cell count and HIV viral load testing at the first HIV-positive visit and follow-up visits (RealTime HIV-1 Viral Load assay; limit of quantification: 40 copies/mL)
- ARV drug testing at the first HIV-positive visit and follow-up visits (using a qualitative assay that detects 20 ARV drugs in five drug classes)
- HIV genotyping at the first HIV-positive visit (ViroSeq HIV-1 Genotyping assay v2.8)

STATISTICAL ANALYSIS

HIV controllers were defined as:

- Viral load <40 copies/mL (elite controller) or <2,000 copies/mL (viremic controllers) at the first HIV-positive visit and at annual study visits (for at least 12 months)
- No ARV drugs detected at those visits

Statistical analysis was performed using SAS 9.4 software. Associations between viral control and participant characteristics were examined using Wilcoxon rank sum tests.

ETHICAL CONSIDERATIONS

Study participants and their parents/guardians provided written consent for participation in the HPTN 068 study. Written assent was obtained for participants younger than 18 years.