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BACKGROUND

The central nervous system is a potential reservoir for HIV in adolescents and young adults (AYA) with perinatal HIV (PHIV). HIV persistence in the central nervous system may impact long-term cognitive outcomes in AYAPHIV.

IMPAACT 2015 examined AYAPHIV with cognitive impairment and receiving effective antiretroviral therapy (ART) to quantify HIV persistence in blood and cerebrospinal fluid (CSF).

HIV DNA was DETECTED in CSF cells from a MAJORITY of adolescents and young adults with PERINATAL HIV INFECTION and cognitive impairment on effective antiretroviral therapy

METHODS

- Study Description:** IMPAACT 2015 was an IRB-approved U.S.-based cross-sectional, multi-site, exploratory, observational study.
- Study Population:** AYAPHIV (13-30 years old) on suppressive ART and with cognitive impairment measured at screening. Cognitive impairment was defined as NIH Toolbox Fluid Cognition Composite standard score >1 S.D. below the normative group mean (<85).
- Study Procedures:** Participants underwent lumbar puncture (LP) to collect at least 8 ml of CSF, as well as phlebotomy and hair collection.
- Study Measurements:**
 - NIH Toolbox was used to assess cognitive function.
 - HIV RNA and HIVgag/pol DNA in blood and CSF were assayed by droplet digital PCR.
 - 11 biomarkers of inflammation and neuronal injury in blood and CSF were quantified by ELISA.
 - Hair was used to quantify ART exposure levels.
 - Exact binomial confidence intervals were calculated, and 41 comparisons evaluated with exact Wilcoxon rank sum tests.

TABLE. Study Participant Characteristics

| Characteristic (N = 18) | Median (Q1, Q3) | Min, Max |
|--|----------------------|--------------|
| Age, years | 20 (18, 23) | 13, 27 |
| Sex | | |
| n (%) female sex at birth | 9 (50%) | na |
| Race | | |
| n (%) Black or African American | 14 (78%) | na |
| Duration of ART, years | 18.3 (16.8, 20.4) | 8, 25.5 |
| Fluid Cognition Composite Score | 68 (59.0, 75.0) | 53.0, 80.0 |
| Pre-entry CD4+ T cell count, cells/uL | 701 (430, 1012) | 143, 1342 |
| CSF leukocytes, cells/uL | 1 (0, 2) | 0, 5 |
| CSF/Plasma Albumin Ratio* | 0.003 (0.002, 0.004) | 0.000, 0.035 |

* Data on one participant not available

RESULTS

FIGURE 1. Prevalence of HIV RNA and DNA in blood and CSF

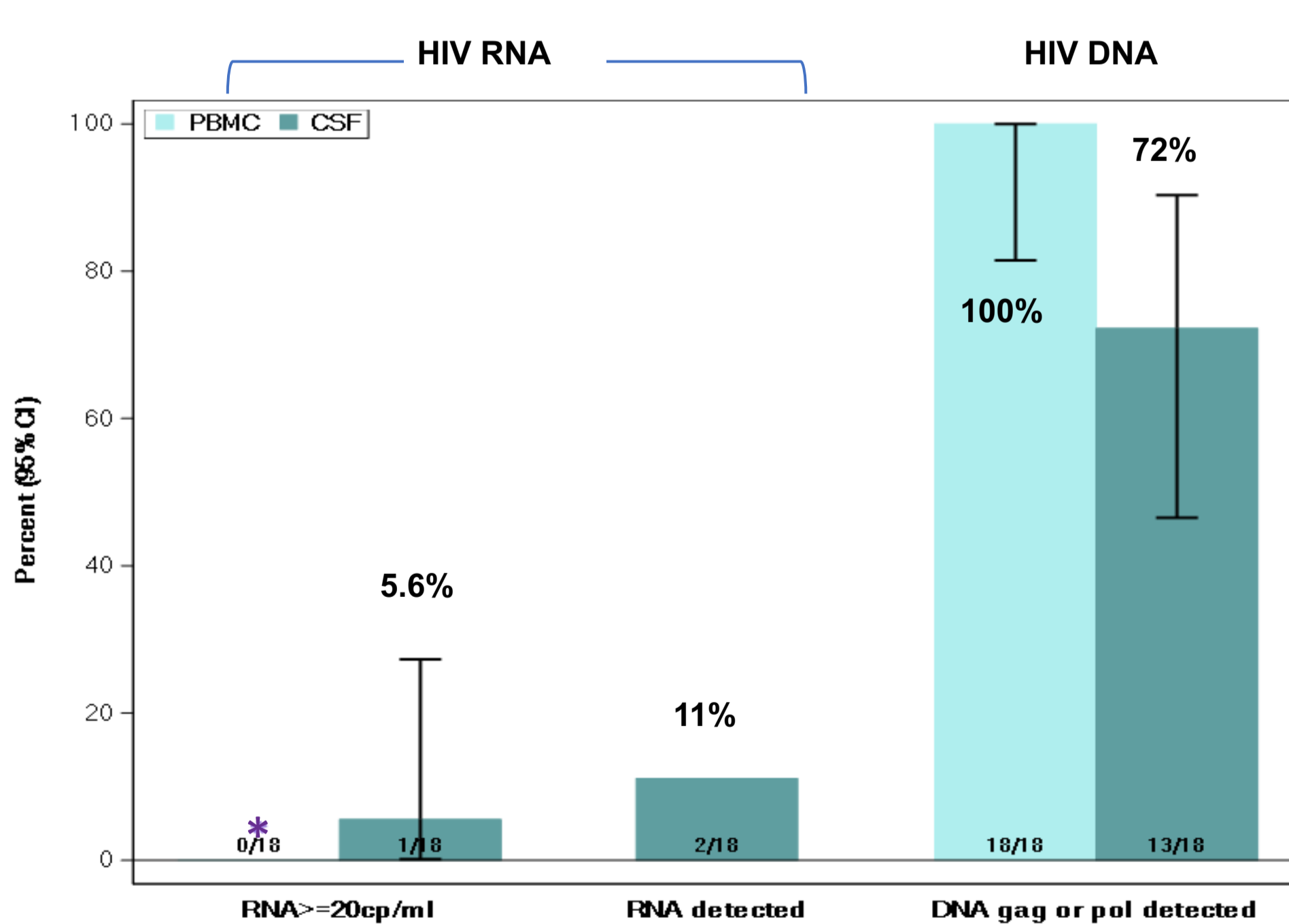


FIGURE 2. Detectable HIV DNA in CSF is associated with higher HIV DNA levels in PBMCs

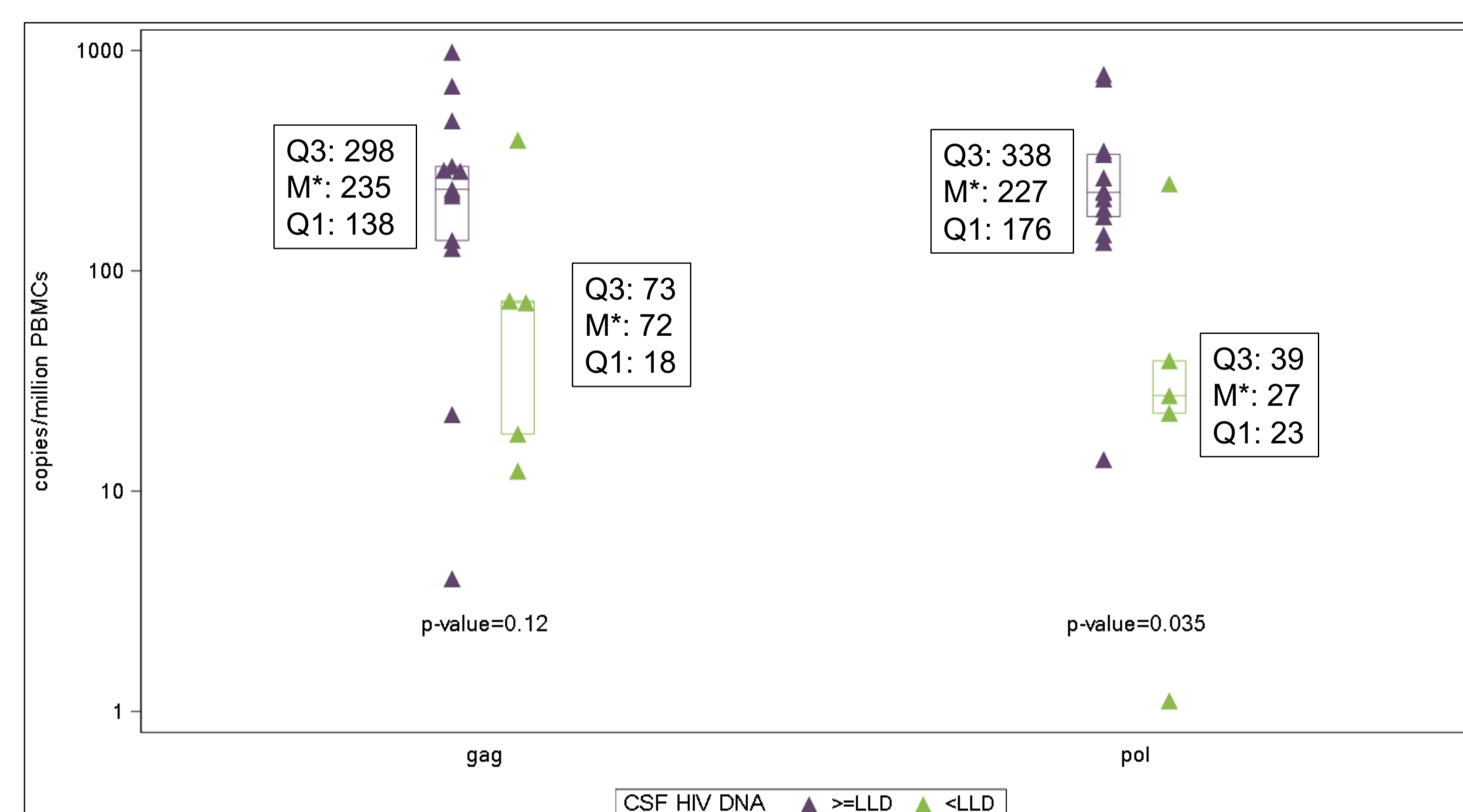
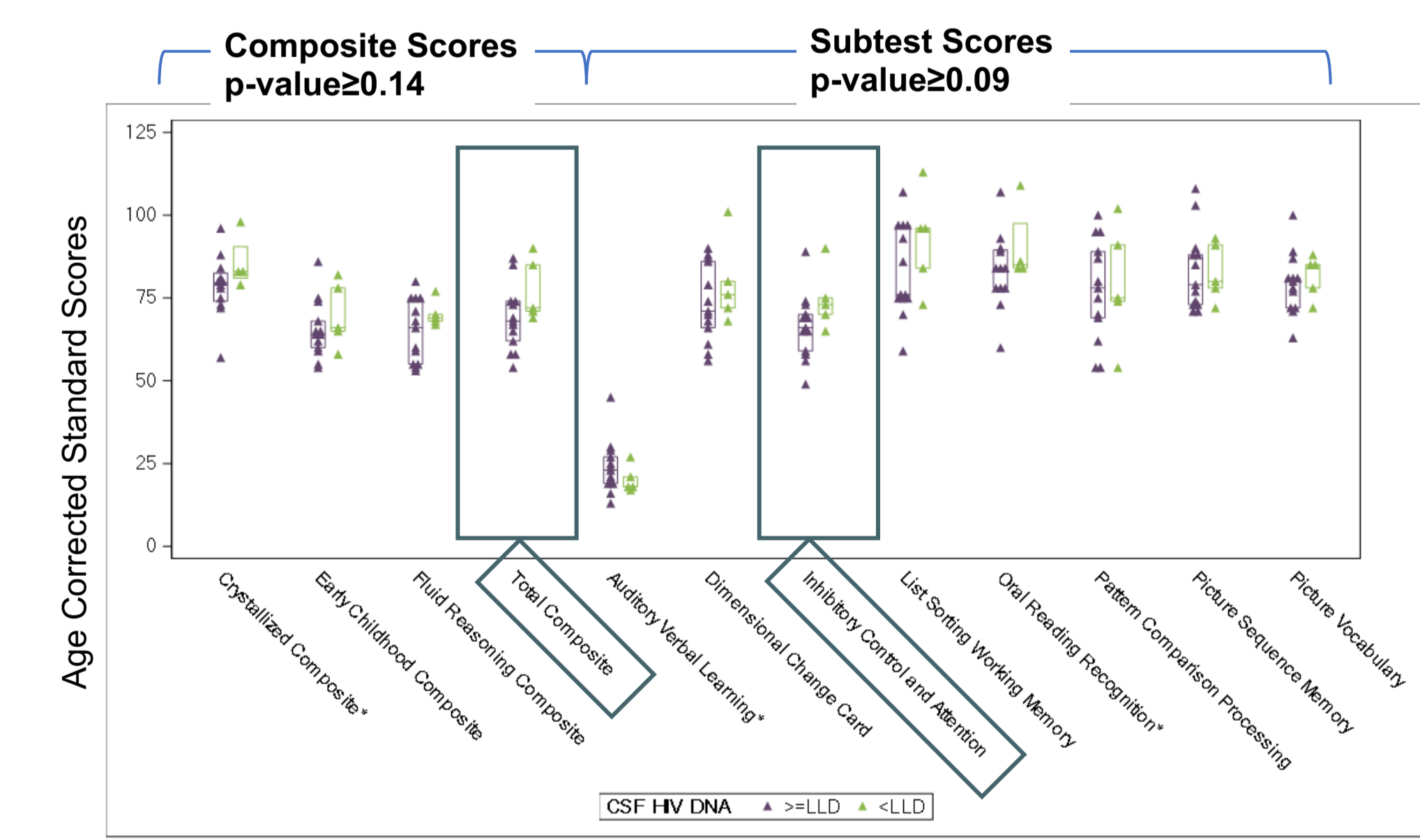


FIGURE 3. Neurocognitive scores trend lower in participants with detectable HIV DNA in CSF



CONCLUSIONS

Among cognitively impaired AYAPHIV on suppressive ART with a median age of 20 years:

- LP is feasible and safe as part of a research protocol
- Quantifiable CSF HIV RNA is infrequent (1/18 participants, 5.6%)
- Detectable CSF HIV DNA is common (13/18 participants, 72%)
- Detectable HIV DNA in CSF is associated with higher HIV DNA levels in PBMCs
- Detectable CSF HIV DNA may be associated with poorer neurocognitive outcomes
- There was no association between detectable HIV in the CSF and plasma/CSF biomarkers of inflammation and neuronal injury or hair antiretroviral drug levels

Pronounced CSF reservoir in AYAPHIV warrants further study

LIMITATIONS

- Small sample size
- Cell numbers interrogated in CSF varied from 94-1950, limiting the sensitivity to detect HIV DNA

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