# COGNITIVE TRAJECTORIES 1 YEAR BEFORE AND AFTER COVID-19 IN AN EARLY TREATED HIV COHORT

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## BACKGROUND

- SARS-CoV-2 infection may have lasting effects on cognition in a subset of individuals
- There are scarce data on the impact of COVID-19 on the objective cognitive performance of people with HIV (PWH)
- We examined the trajectory of cognitive performance 1 year before and after COVID-19 in the RV254 acute HIV study in Thailand

## METHODS

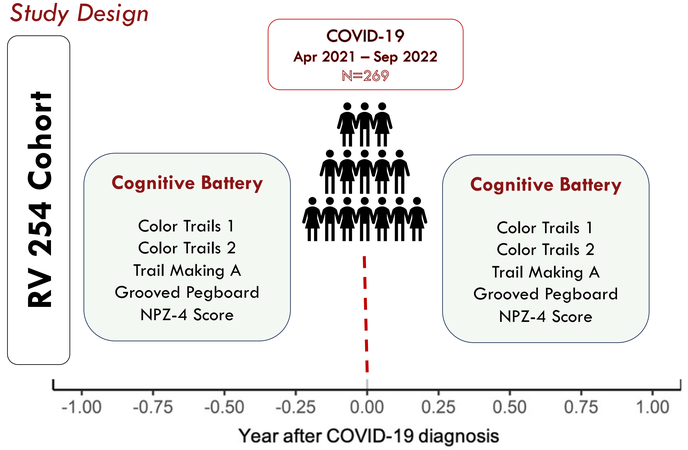
*Participants*

- RV254/SEARCH010 participants on ≥ 48 weeks of stable ART diagnosed with COVID-19 between April 2021 and September 2022 (n=269)

*Cognitive Battery*

- ***Color Trails 1 & 2 (CT1, CT2):*** Psychomotor Speed and Executive Function
- ***Trail Making A (TMA):*** Psychomotor Speed
- ***Grooved Pegboard, non-dominant hand (GPB):*** Fine Motor Speed/Dexterity
- Raw scores were converted to demographically-adjusted z scores using locally-derived norms.
- ***NPZ-4 score:*** aggregate z-score for the 4 cognitive tests

*Study Design*




*Statistical Analysis*

- Cognitive test z-scores **1 year pre- and post-COVID-19** were regressed on time using linear mixed models.
- Time in years since COVID-19 diagnosis was entered as a linear spline with knots at the time of COVID-19 diagnosis and 0.25-year intervals thereafter; each timepoint after diagnosis was compared with the value at diagnosis
- Statistical analyses were performed using SAS Studio, version 3.8 (Cary, NC), and RStudio, version 4.2.2.

**In a cohort of PWH on suppressive ART, there are modest but significant declines in processing speed & overall cognitive performance up to 6 months after acute COVID-19**

## RESULTS

**Table 1** Characteristics of RV254 participants with COVID-19 between April 2021 and September 2022

| Characteristics | N=269 |
|---|---|
| Age at COVID-19 diagnosis, *median (IQR)* | 32 (29 - 37) |
| Male, n (%) | 261 (97%) |
| Duration from ART initiation to COVID-19 (yrs), median (IQR) | 6 (4.7 – 7.9) |
| CD4+ T-cell count, *median (IQR)* | 688 (570, 865) |
| HIV RNA > 50 copies/mL prior to COVID-19, n (%) | 5 (2%) |
| **COVID-19 vaccine doses received prior to COVID**, n (%) | |
| 0-1 | 40 (15%) |
| 2-3 | 185 (69%) |
| ≥ 4 | 44 (16%) |
| **Time period diagnosed (predominant variant of concern), n (%)** | |
| Sep 2020 – Mar 2021 | 1 (0%) |
| Apr 2021 – June 2021 (Alpha/beta) | 13 (5%) |
| Jul 2021 – Dec 2021 (Delta) | 34 (13%) |
| Jan 2022 – Sep 2022 (Omicron) | 221 (82%) |
| Supplemental Oxygen | 4 (1.5%) |
| Mortality | 0 (0%) |

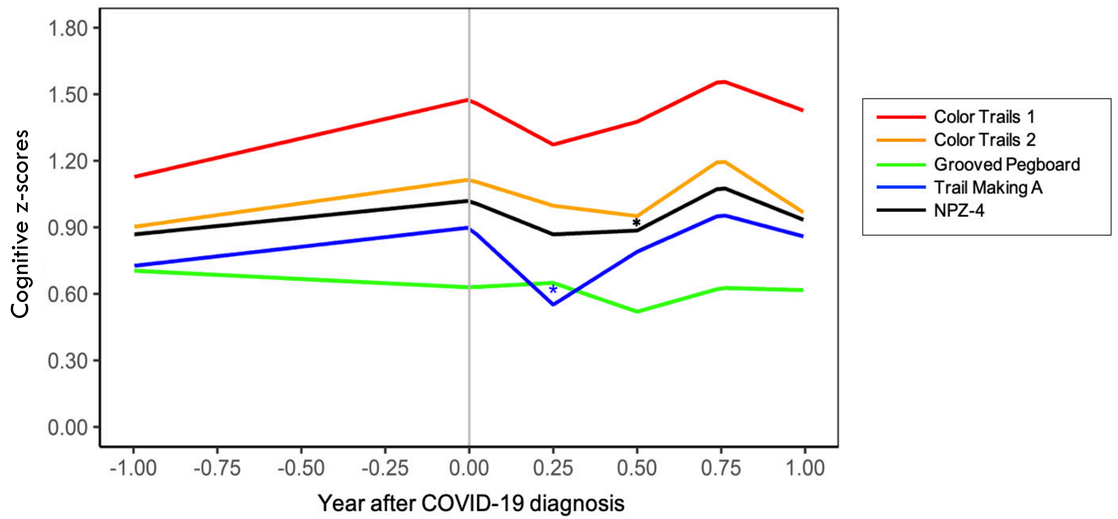



**Figure 1**. Cognitive z-scores 1 year before and after COVID-19 diagnosis. *P-Value < 0.05
Note: Values at 0.25, 0.50, 0.75, and 1.00 years were compared to values at 0.00 years

## SUMMARY OF FINDINGS

- Between April 2021 and September 2022, **269** participants on >48 weeks of stable ART were diagnosed with COVID-19
  - 82% (n=221) had COVID-19 during the Omicron wave
  - 85% (n=229) received ≥2 doses of COVID-19 vaccine doses prior to diagnosis
  - 4 (1.5%) required supplemental oxygen
- Compared with values at the time of COVID-19 diagnosis, there were **significant transient declines** in
  - **TMA z-score at 3 months:** 0.90 vs. 0.55 (p=0.02)
  - **NPZ-4 score at 6 months:** 1.02 vs. 0.89 (p=0.03)
- Similar trends were observed for the other cognitive tests (CT1, CT2, and GPB) but the p values were > 0.05.

## CONCLUSIONS

- In this cohort of young, mostly male, virologically suppressed PWH who initiated ART during AHI, we observed **modest but significant changes** on one test of **psychomotor speed and,** relatedly, the **NPZ-4 score,** up to **6 months after acute COVID-19**
- These findings highlight the need for longer-term follow-up and monitoring of post-acute cognitive sequelae of COVID-19 in PWH
- Longitudinal assessments of brain MRI and soluble immune markers in cerebrospinal fluid are ongoing to further characterize the impact of COVID-19 on cognitive outcomes in this early-treated HIV cohort

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