

Longitudinal Monitoring of Alzheimer's-Related Cognitive and Psychiatric Symptoms in a Post-COVID Cohort

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Background:

- Long-term neuropsychiatric sequelae of COVID-19 have raised concerns regarding accelerated cognitive decline and increased vulnerability to neurodegenerative processes, including those related to Alzheimer's disease.
- Cognitive domains typically affected in Alzheimer's disease—such as memory and language — have been reported as potentially impaired following COVID-19. In parallel, persistent psychiatric symptoms may confound or mimic early neurodegenerative presentations.

Objective:

- This study aimed to characterize longitudinal changes in cognitive performance and psychiatric symptoms in a cohort of COVID-19 survivors, with particular emphasis on metrics relevant to Alzheimer's-related cognitive trajectories.

Methods:

- A total of 361 adults (162 females, 199 males; mean age 54.9 ± 13.4 years) previously hospitalized for COVID-19 in Brazil underwent repeated follow-up.
- Cognitive evaluation included standardized test of memory (CERAD battery), i.e., Immediate Memory and Verbal Recognition as well as three levels of language Boston Naming Tests.
- Psychiatric outcomes were assessed using Hospital Anxiety and Depression Scale (HADS), and post-traumatic stress symptoms (PTSS).
- Longitudinal changes were analysed using linear regression models, adjusting for age, sex, and severity of acute illness. Effect sizes and 95% confidence intervals were calculated to quantify within-subject change over time assessments between 2020 and 2024.

Results:

- In cognitive evaluation measures, i.e., Immediate Memory improved by 0.38 units per year (95% CI: 0.16–0.59; $p = 0.001$), while verbal recognition improved by 0.25 units per year (95% CI: 0.13–0.36; $p < 0.001$).
- Among language measures, a significant decline was detected in medium-difficulty composite (Boston MED: -0.12 units per year; 95% CI: -0.17 to -0.07 ; $p < 0.001$), whereas the low- and high-difficulty composites remained stable over the four-year follow-up period.
- Regarding psychiatric outcomes, Anxiety and PTSS showed significant gradual improvement, decreasing by -0.30 (95% CI: -0.52 to -0.06 ; $p = 0.015$) and -0.12 (95% CI: -0.16 to -0.07 ; $p < 0.001$) points per year, respectively.
- Depressive symptoms did not demonstrate a significant longitudinal change.

Conclusions:

- Overall, Alzheimer's-related psychiatric and cognitive metrics demonstrated either significant improvement or stability over four years of follow-up, after accounting for age and sex (except in Boston MED). These findings suggest preserved or recovering cognitive trajectories in most domains following COVID-19, with limited evidence of progressive decline (Figure 1).

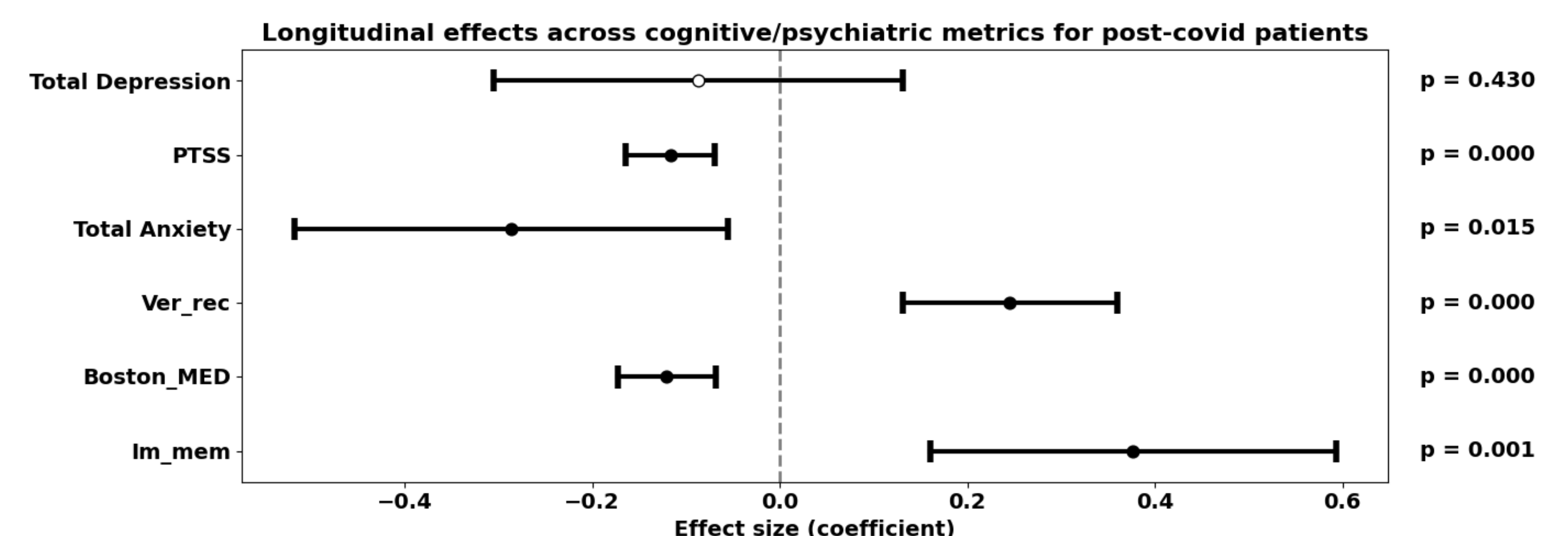


Figure 1. Age- and sex-adjusted longitudinal changes in Alzheimer's-related psychiatric and cognitive metrics in post-COVID-19 patients over four years. **Total Depression**= summation of 7 measures for rated from 0 to 3 for each of following key words: enjoy, smile, cheerful, slow work, taking care of appearance, lively, pleasure, **PTSS**= summation of 7 measures for rated from 0 to 5 for each of following key words: stressful experience from the past, irritation, stress, sleep problem, disappointment, hyper-alert, startled, **Total Anxiety**=summation of 7 measures for rated from 0 to 3 for each of following key words: tense, contracted, a kind of fear, worries, restless, anxious, panic, **Ver_rec**= verbal recognition of three list of words, **Boston_MED** = Selective decline in moderately demanding lexical access (medium frequency), **Im_mem**=Immediate memory of 20 words.