Immediate and long term cognitive improvement after cognitive vs. emotion management psychoeducation programs

A randomized trial in COVID patients with neuropsychological difficulties

COVCOG Study

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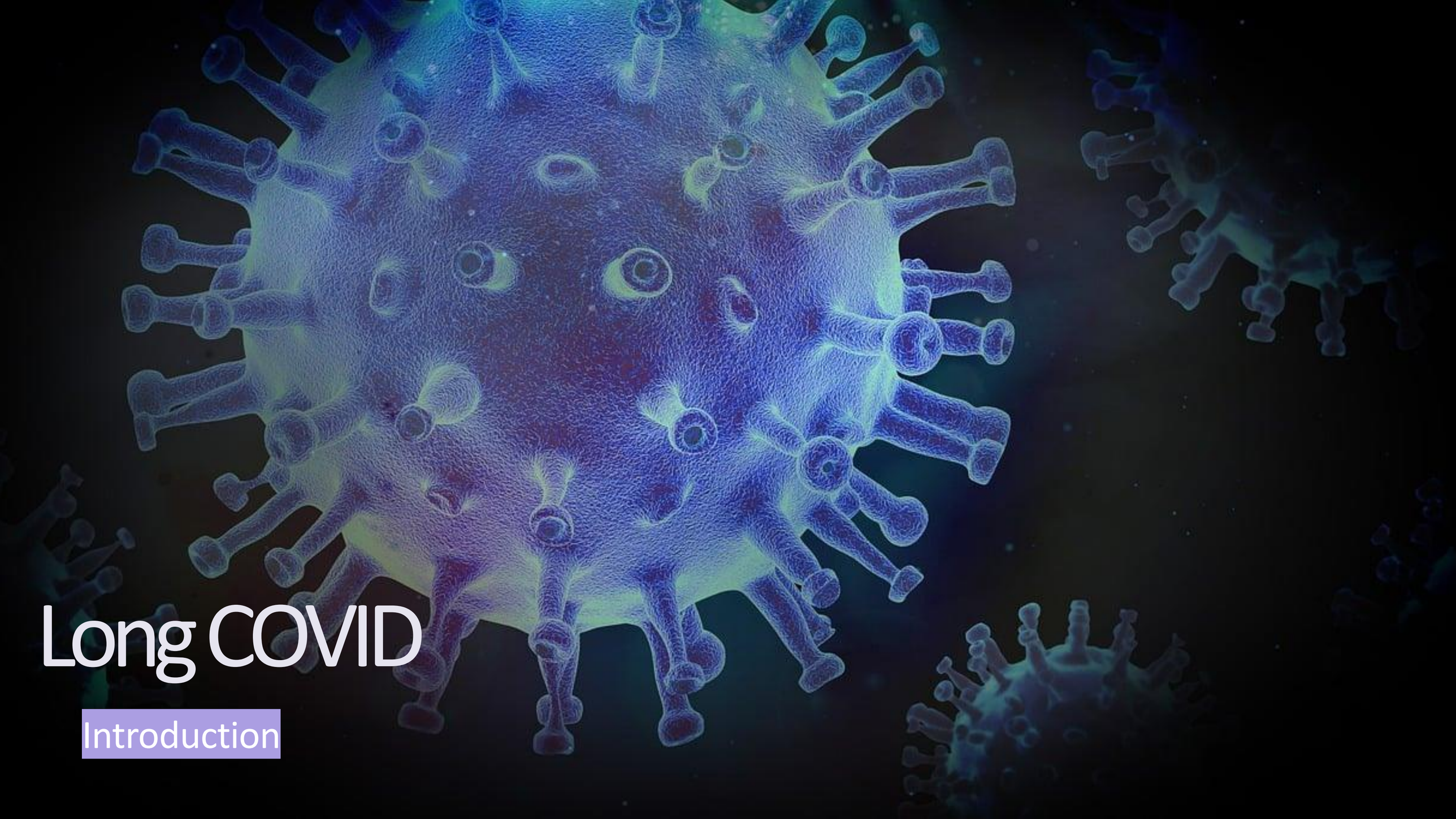


Long COVID

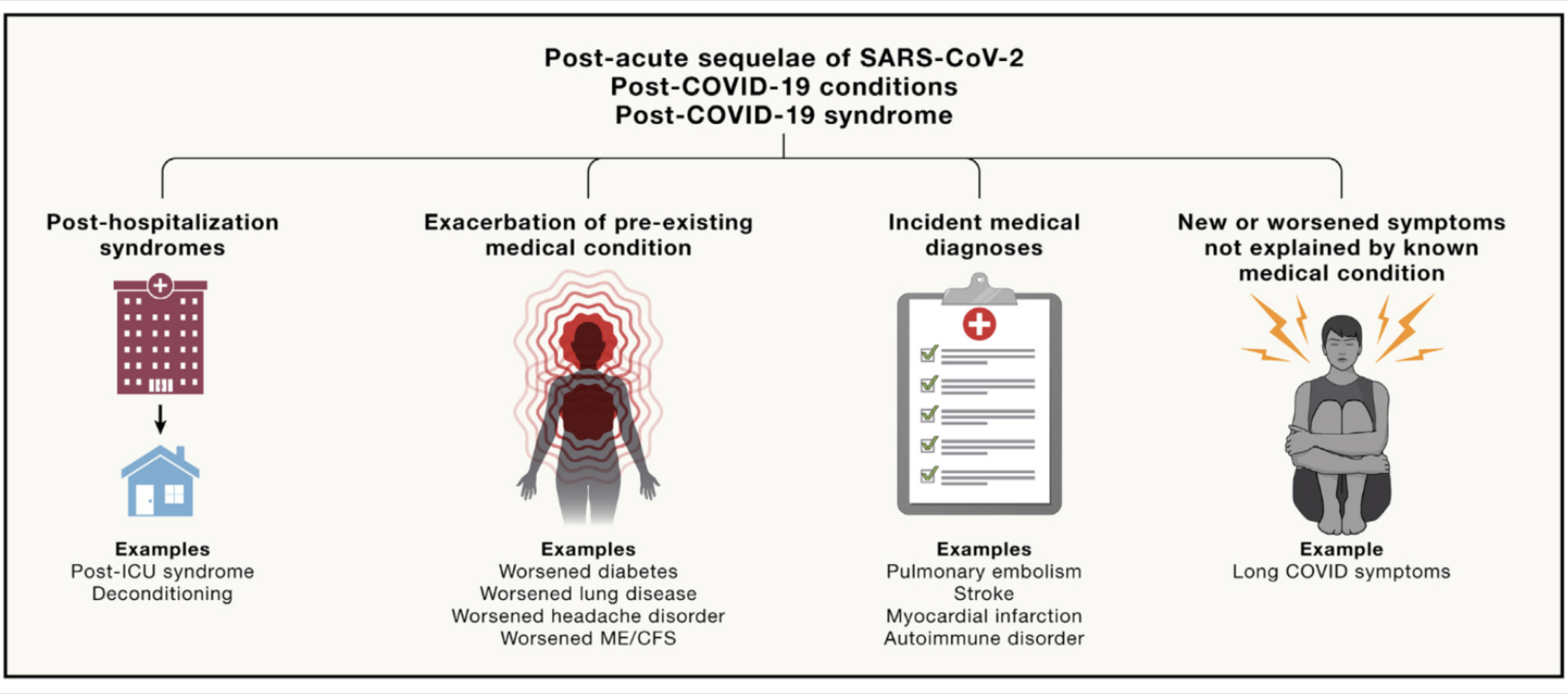
Introduction

Multiple terminologies

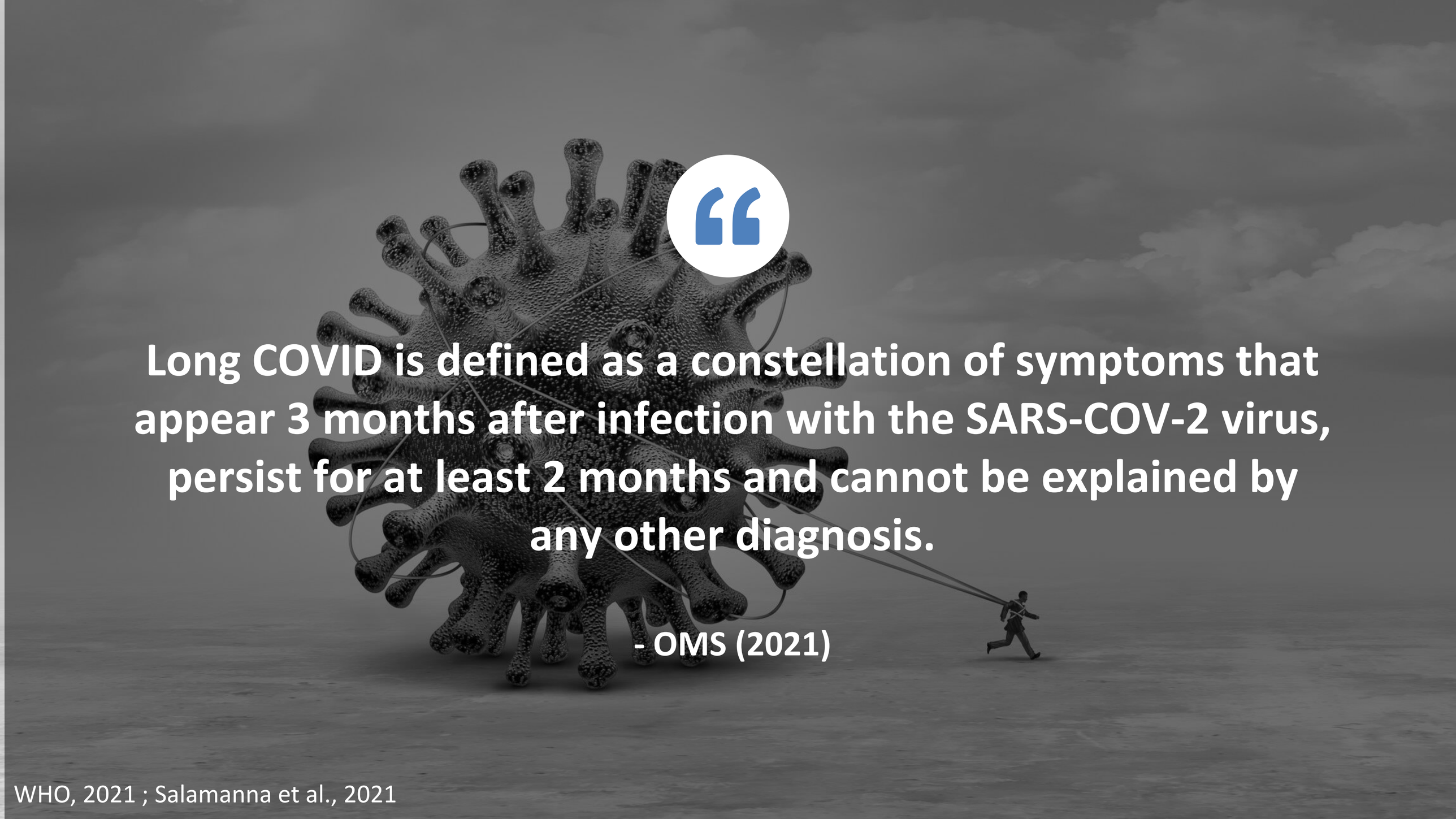
Terminology	Persistence of symptoms after C-19
Long-COVID -19	> 8 weeks, without association with other existing pathologies; post-C19 with persistent symptoms > 12 weeks (NICE)
Long-term C19	> 4-12 weeks
Post-C19	> 8 weeks
Post-acute sequelae of COVID-19 (PASC)	>4 weeks after the first signs
Persistent post - C19	> 24 weeks
Long-haul C19	> 100 days

Gheorghita, et al., 2024

Long COVID



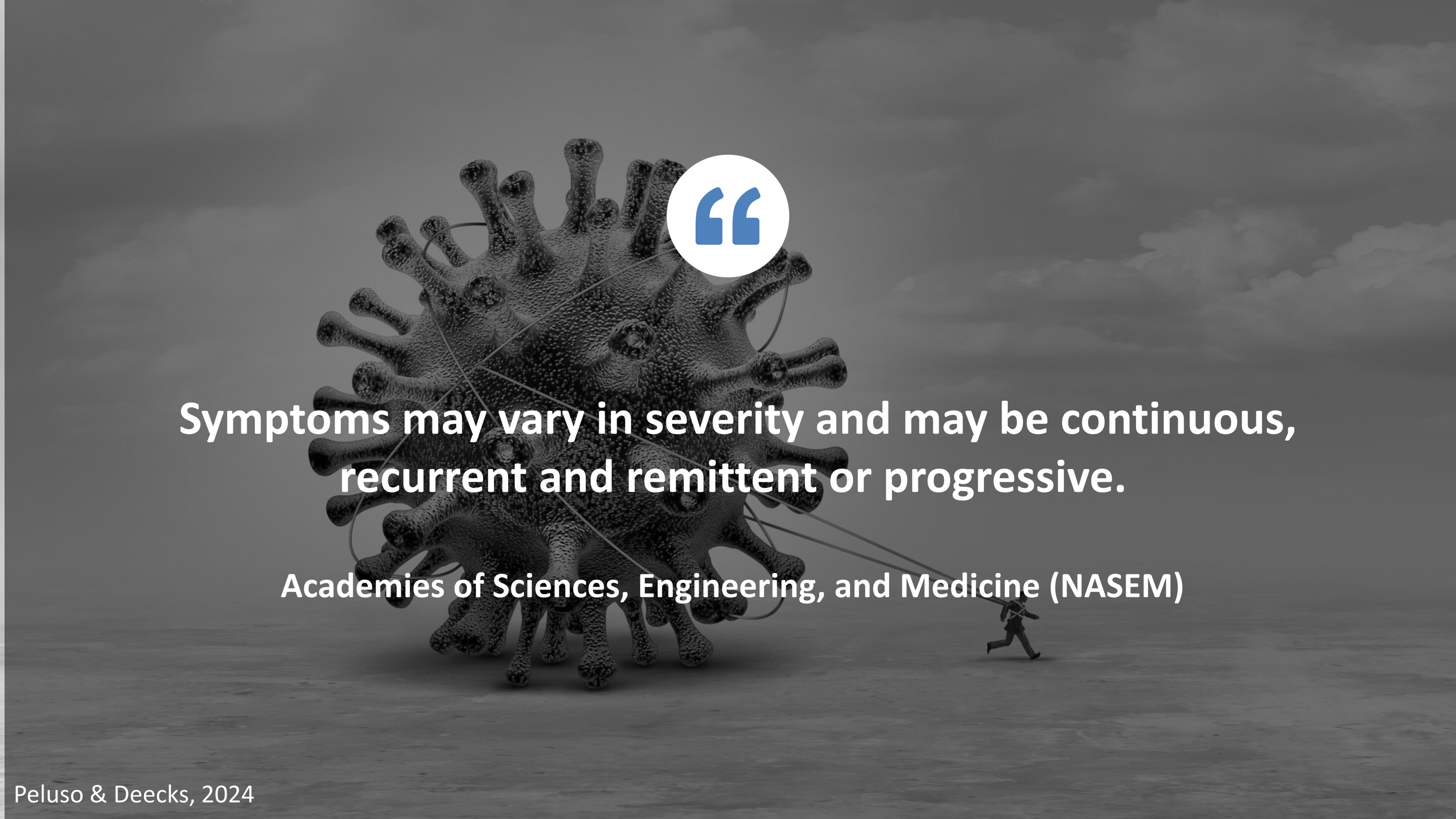
Peluso & Deecks, 2024



Long COVID is defined as a constellation of symptoms that appear 3 months after infection with the SARS-COV-2 virus, persist for at least 2 months and cannot be explained by any other diagnosis.

- OMS (2021)

WHO, 2021 ; Salamanna et al., 2021



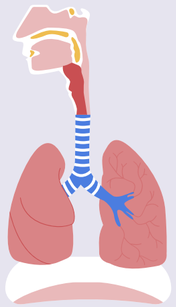
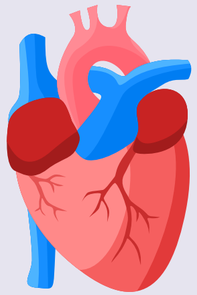
Symptoms may vary in severity and may be continuous, recurrent and remittent or progressive.

Academies of Sciences, Engineering, and Medicine (NASEM)

Peluso & Deecks, 2024

Manifestations of Long COVID

- Multisystemic syndrome affecting several organic systems :

- Fatigue and cognitive difficulties are among the most common reported symptoms
  - Subjective complaints (i.e. concentration, memory, multitasking)
  - Objective impairment (i.e. attentional, memory, executive)

Mehandru et Merad, 2022 ; Salamanna et al., 2021; Liu et al., 2023 ; Han et al., 2022; Tavares-Júnior et al., 2022

Long COVID

Prevalence

70 %

At least one symptom at short term

i.e. 2 months or more after the onset of infection

(see Nasserie et al., 2021)

60 %

At least one symptom at long term

ci.e. 12 months or more after the onset of the infection (most commonly fatigue, dyspnea et anxiety; Fischer et al., 2022)

30 %

Chronic

Improvement observed, but 30% still report symptoms affecting daily life (related to cognition, sensorimotor function and mental fatigue) (Wahlgrend et al., 2023) Evolution and stabilisation unknown

Pathophysiology of Long COVID

- Complex interplay of factors from different aetiologies

Direct viral infection of CNS

Hypoxia

Maladaptive inflammatory response

Neuropsychiatric comorbidities

Dysfunction of the autonomic nervous system

Politi et al., 2020 ; Dondaine et al., 2022 ; Najjar et al., 2020; Wu et al., 2024; Molnar et al., 2024 ; Poletti et al., 2022 ; Dani et al., 2021

Long COVID

Prevalence - cognitive complaints

>30% report cognitive problems one month after recovery (Liu et al., 2023).

>20% > 3 months (Han et al., 2022)

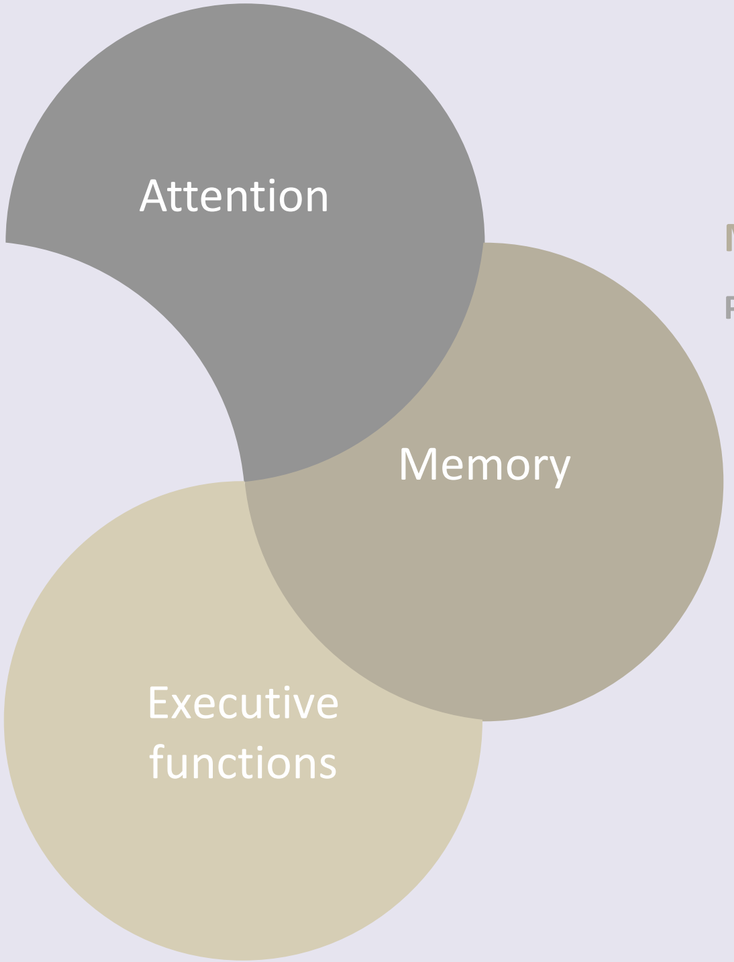
> 15 % > 12 months (Han et al., 2022) / More than 30% (if hospitalisation) >24 months (Wahlgrend et al., 2023)

Long COVID

Objective cognitive impairment

Attention

The sensation of being slowed down, difficulty concentrating, sensitivity to interference, difficulty with double tasks....



Memory

Prospective memory; short- and long-term memory

Executive functions

planning and organization

Association between subjective and objective measures

Inconsistent association :

- In some cases, a correlation is observed (García-Sánchez et al., 2022)
- In other cases, these two measures are not associated (Gouraud et al., 2021 ; Bland et al., 2024).

Long COVID

Factors and biasis

Good Old Days

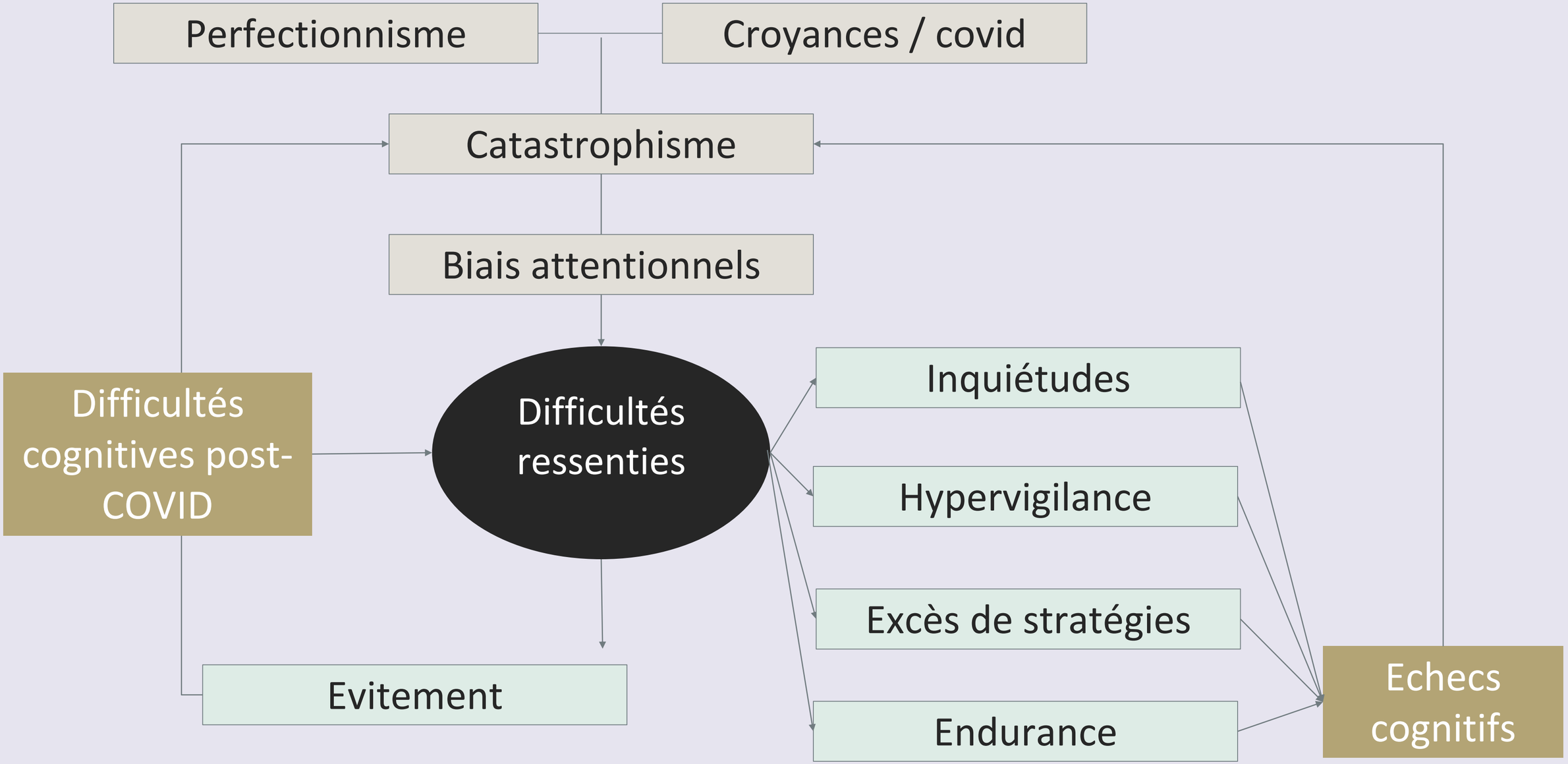
L’évitement des situations problématiques

L’endurance excessive

Les biais attentionnels

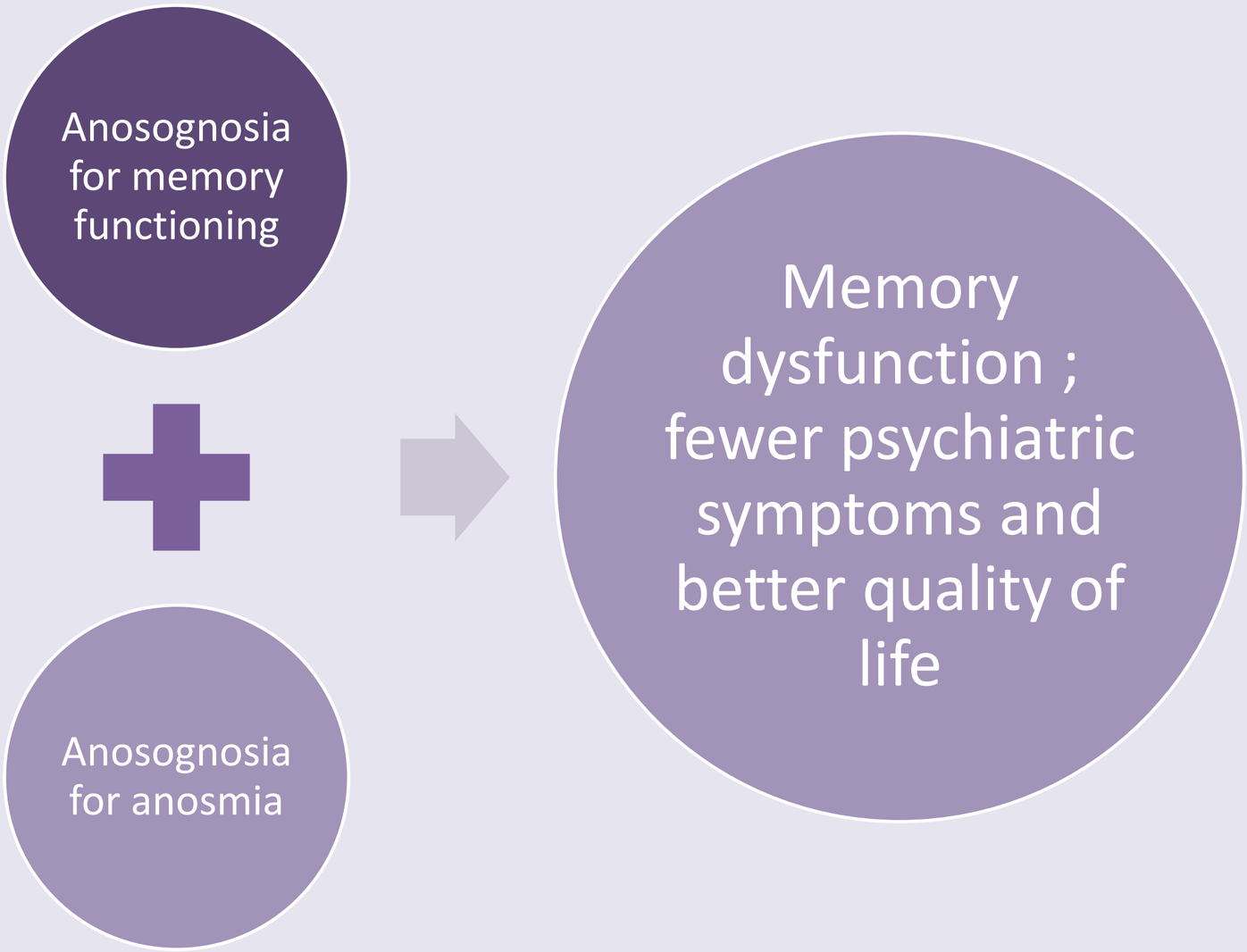
Les biais métacognitifs

Long COVID



Inspiré de Silverberg & Rush, 2024

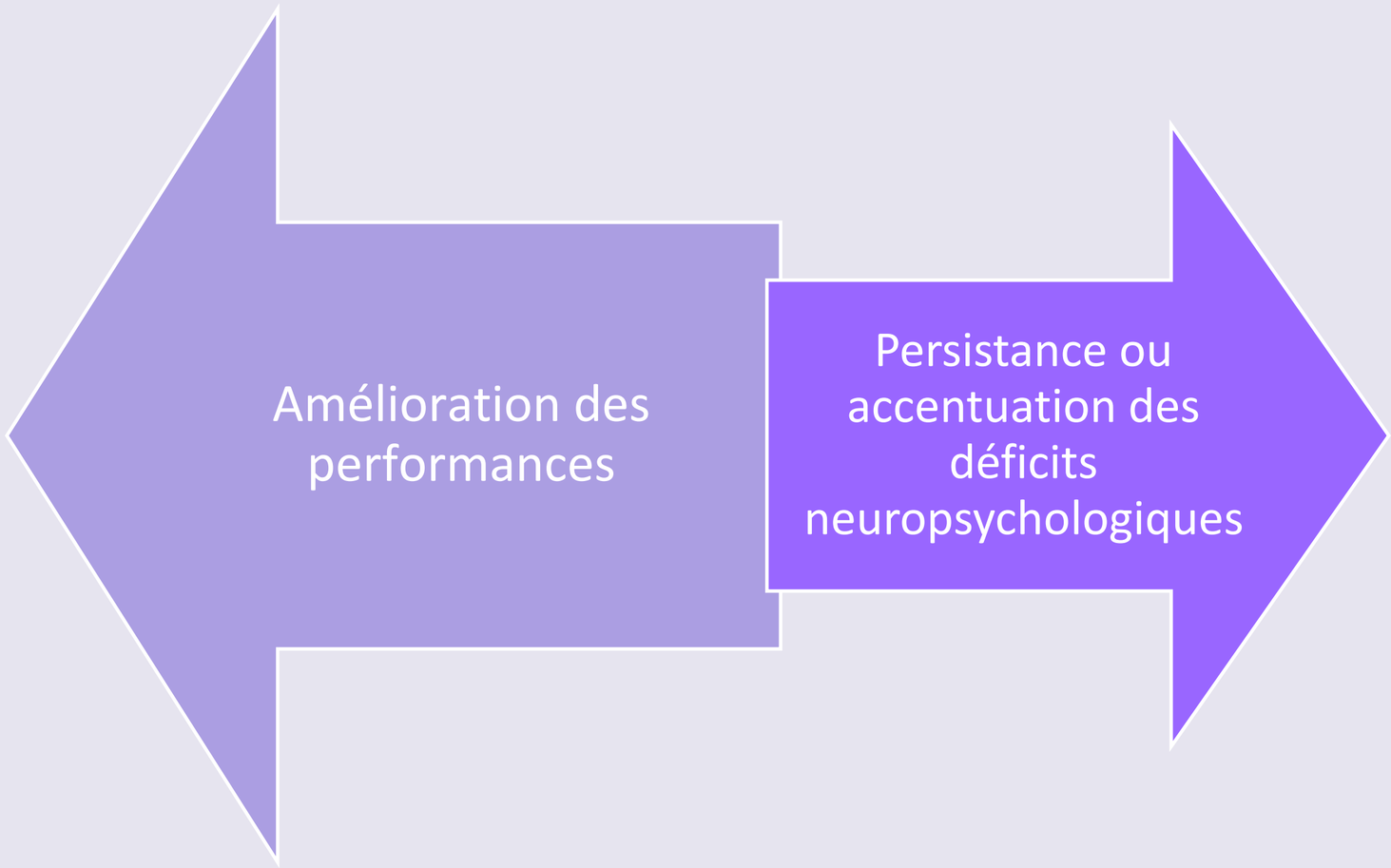
Different cognitive profiles



Voruz et al., 2022; 2024

Long COVID

Different cognitive profiles - Distinct recovery trajectories



Voruz et al., 2022; 2024

What are the treatment options ?

- Adaptation of pre-existing therapies (i.e. cognitive rehabilitation programs in ABI or PCS)

- Multiplicity of symptoms, including psychological factors = Cognitive Behavioural Therapy (CBT)

Mathern et al., 2022; Tay et al., 2021

Objective

What is the most effective psychoeducational intervention (cognitive vs. affective) for Long COVID patients with cognitive complaints ?
(2 months follow-up evaluation)

Hypothesis :

Superior efficacity expected with a cognitive approach

COVCOG Study

Effects of two interventional programs (cognitive vs. affective psychoeducation) in Long COVID patients with cognitive difficulties

COVCOG Study

Willems *et al. BMC Neurology* (2023) 23:307
https://doi.org/10.1186/s12883-023-03346-9

BMC Neurology

STUDY PROTOCOL Open Access

COVCOG: Immediate and long-term cognitive improvement after cognitive versus emotion management psychoeducation programs - a randomized trial in covid patients with neuropsychological difficulties

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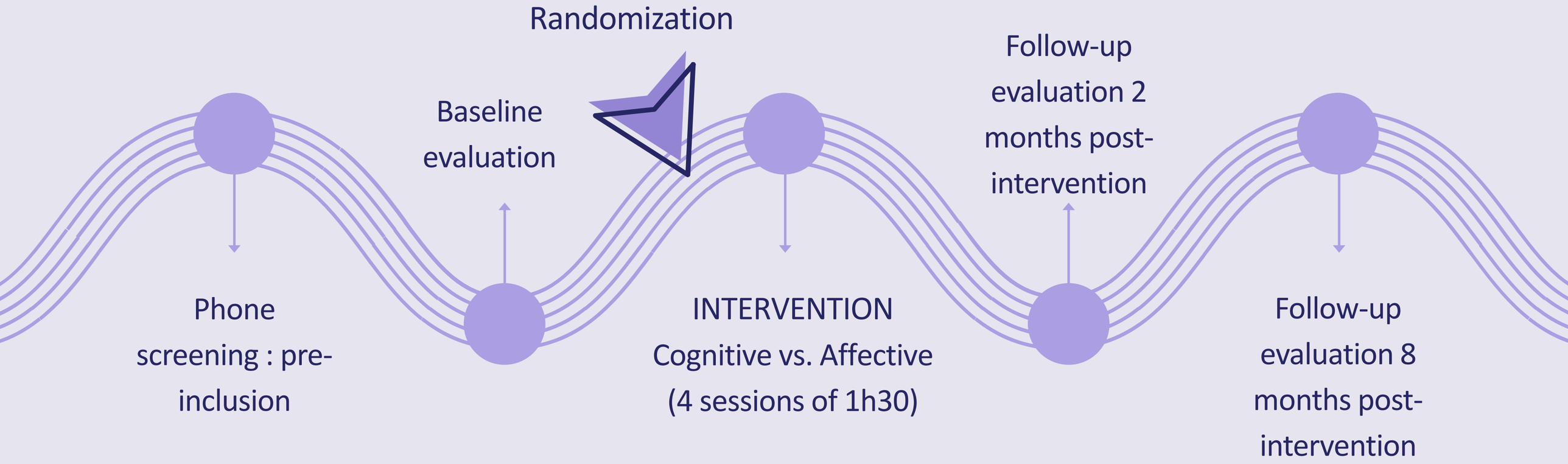
- Pre-registration (clinicaltrials.gov: NCT05167266)
- Randomized Control Trial (RCT)
- Data collection between March 2022 and June 2024
- N=130 randomized in either cognitive or affective intervention (ratio 1:1)
- Cognitive complaints at least 3 months after SARS-CoV-2 infection

Willems et al., 2023

COVCOG Study

Chronology of the study (10.5 months)



COVCOG Study

Neuropsychological evaluation

Cognitive assessment

- Memory
- Attention
- Executive functions
- Langage

Self-reported questionnaires

Primary outcomes = cognitive complaints

- **Executive control (BRIEF-A)**
- **Memory functioning (MMQ)**

- Fatigue
- Sleep difficulties
- Quality of life
- Psychological distress
- Impact on daily activites

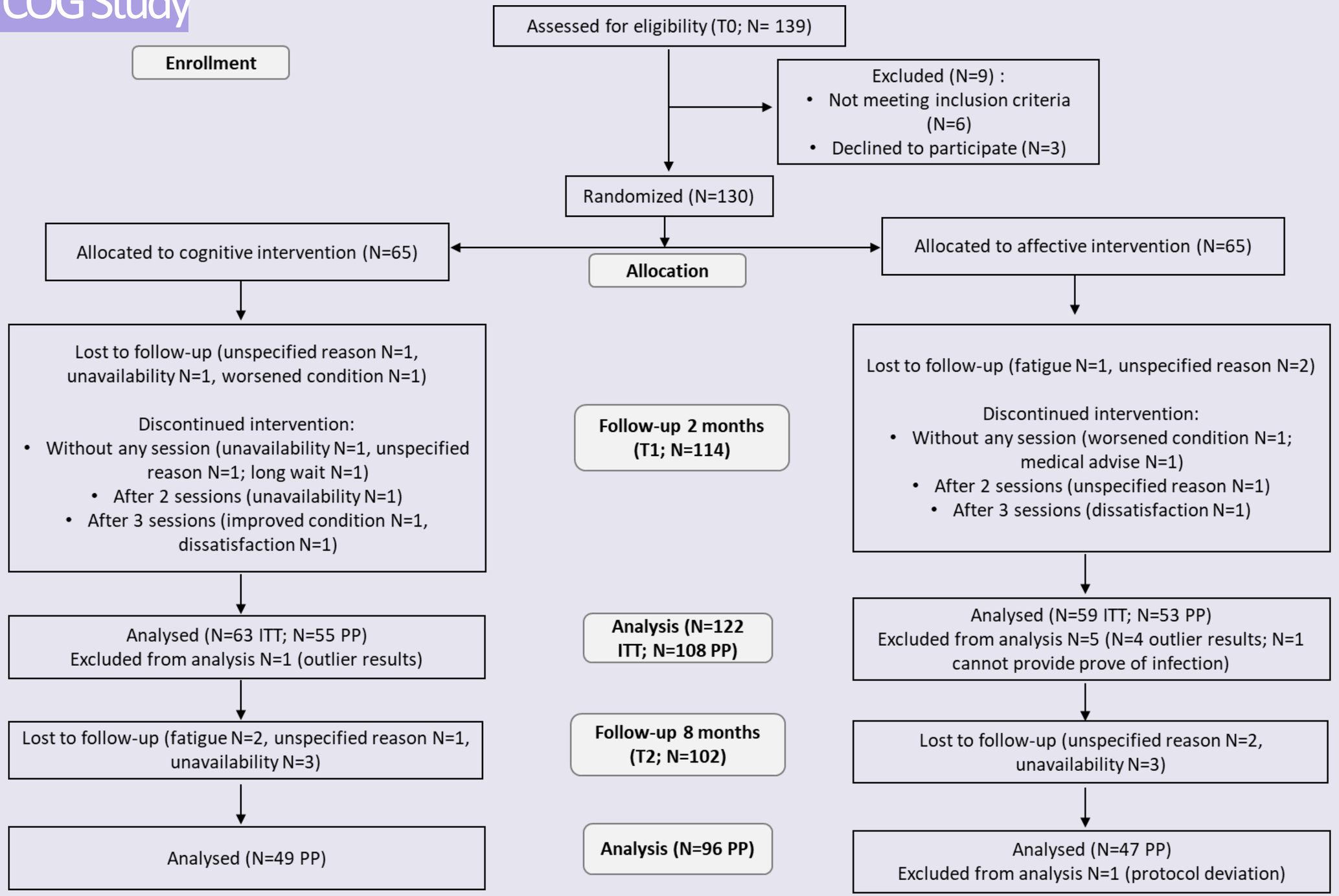
Cognitive intervention

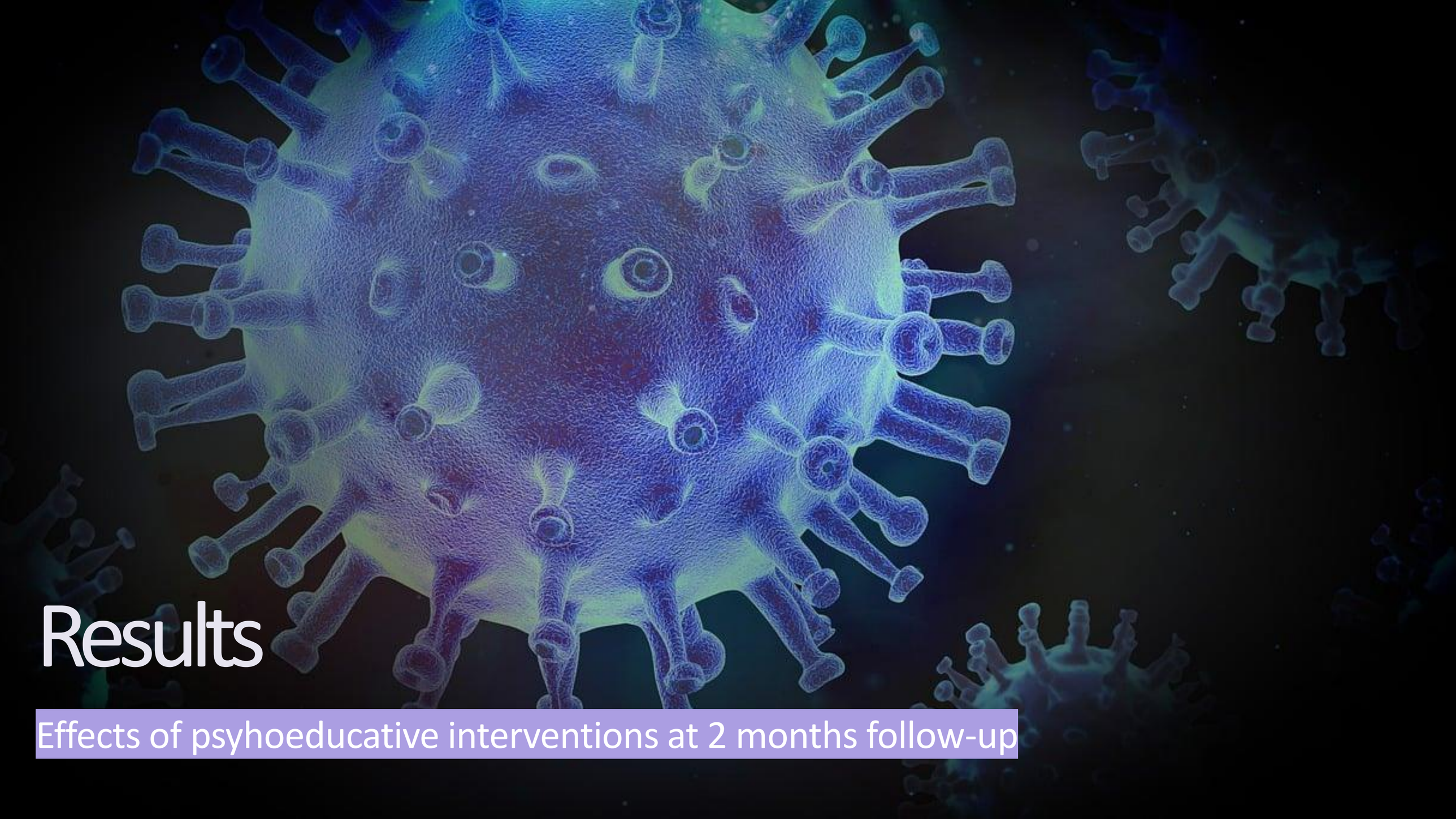
- 4 sessions of 1h30 + reactivation session of 30 min (after 1 month)
- Intensified by videotherapy and home exercices
- Psychoeducation targeting metacognition to teach appropriate behaviours and strategies

Affective intervention

- 4 sessions of 1h30 + reactivation session of 30 min (after 1 month)
- Intensified by relaxation exercises, notes and home exercises
- Psychoeducation targeting self-efficacy for emotions management and regulation of behaviours impacting the perception of difficulties on daily living activites

COVCOG Study





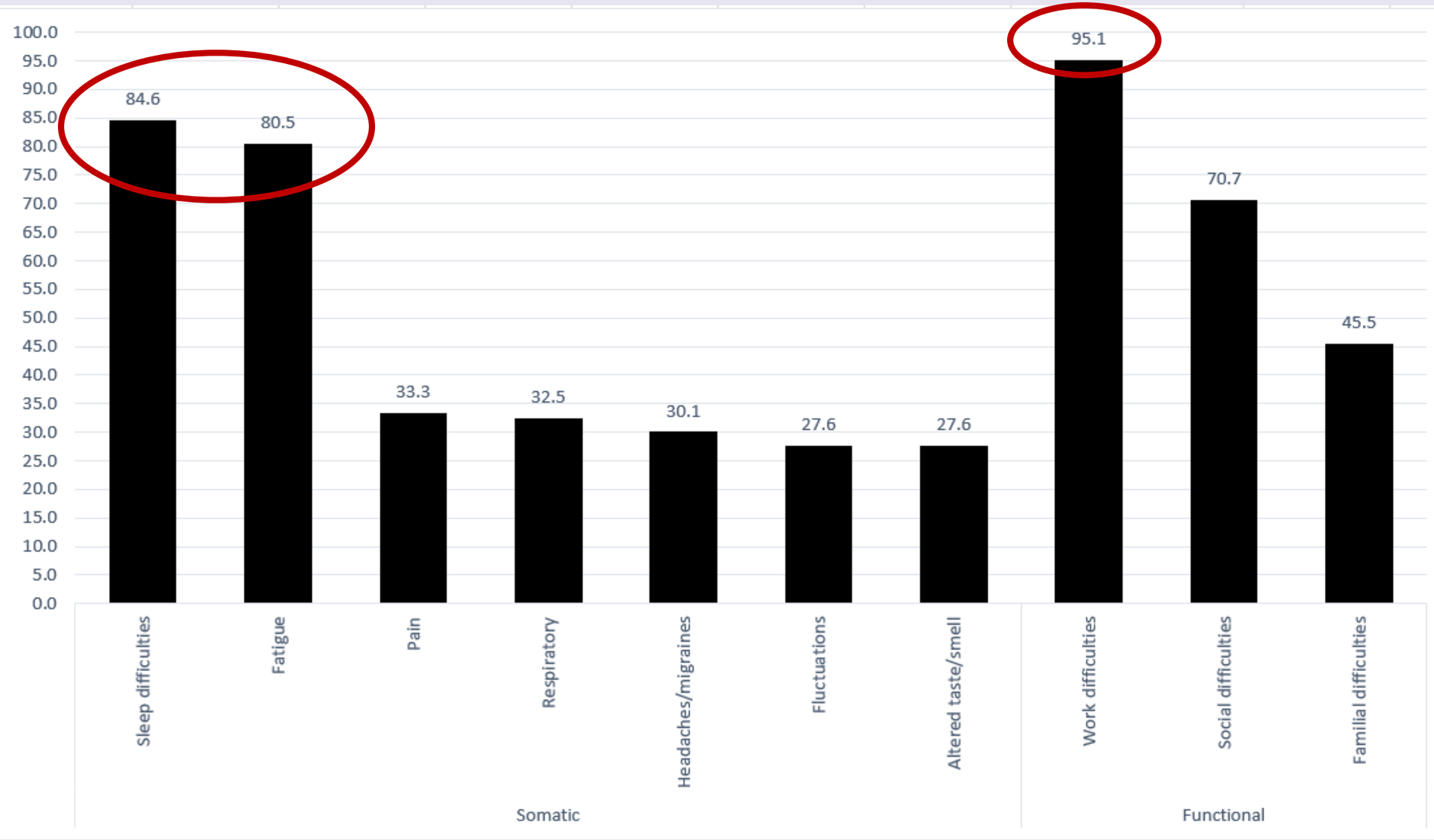
Results

Effects of psyhoeducative interventions at 2 months follow-up

Results

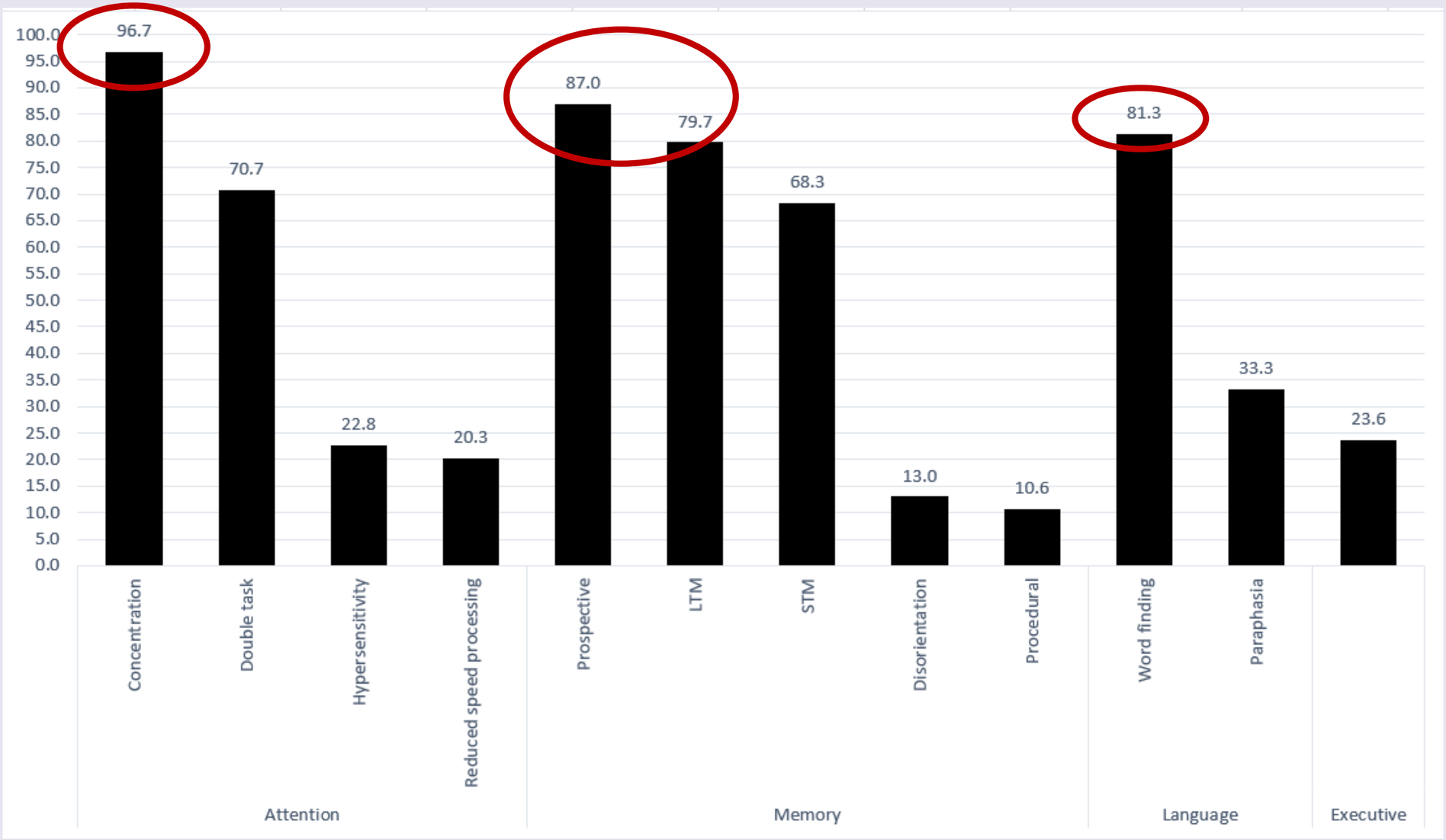
		Total
Demographics	Age (mean ± SD) [range]	47 ± 10 [21-66]
	Sex (female)	85 (69.7%)
	Years of education (mean ± SD) [range]	14 ± 3 [6-17]
History of COVID-19	Asymptomatic	1 (0.8%)
	Mild infection	67 (54.9%)
	Moderate infection	41 (33.6%)
	Severe infection	13 (10.7%)
	Hospitalized	16 (13.1% ; 10 female)
	ICU treatment; mean stay	8 (6.6% ; 3 female) ; 13 days
	Number of infections (mean ± SD) [range]	1.7 ± 0.9 [1-5]
	Time since first infection (months)	20.9 ± 8.6 [4-39]

Baseline evaluation – Somatic and functional complaints spontaneously reported



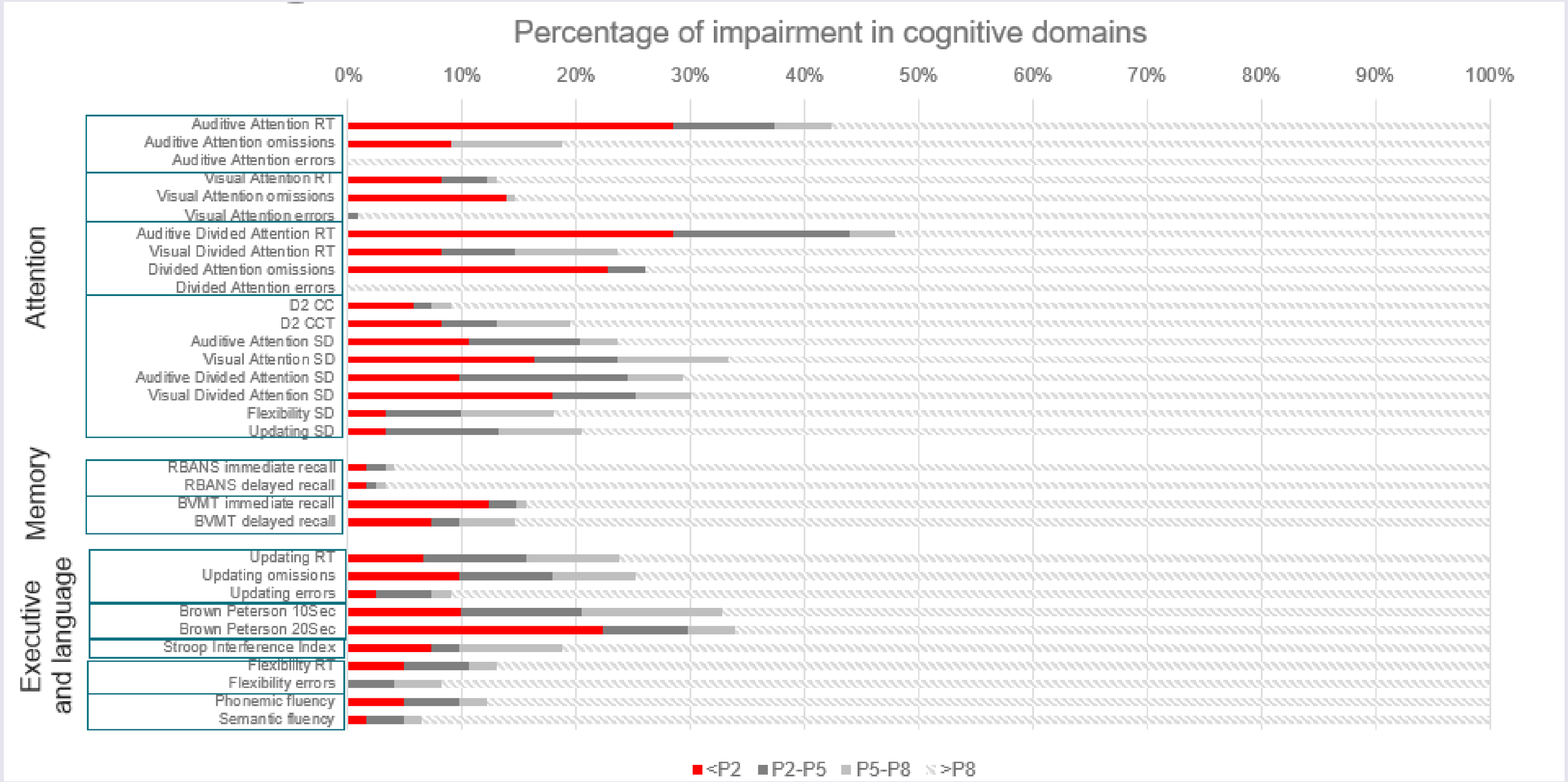
Results

Baseline evaluation – cognitive complaints spontaneously reported



Results

Baseline evaluation – objectivation

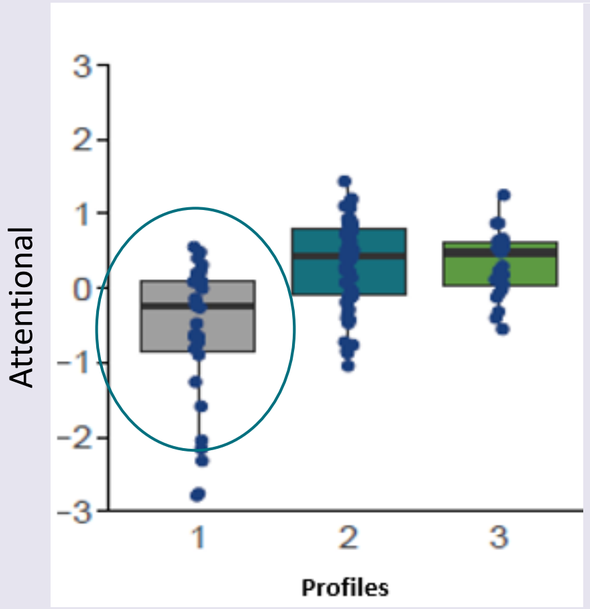


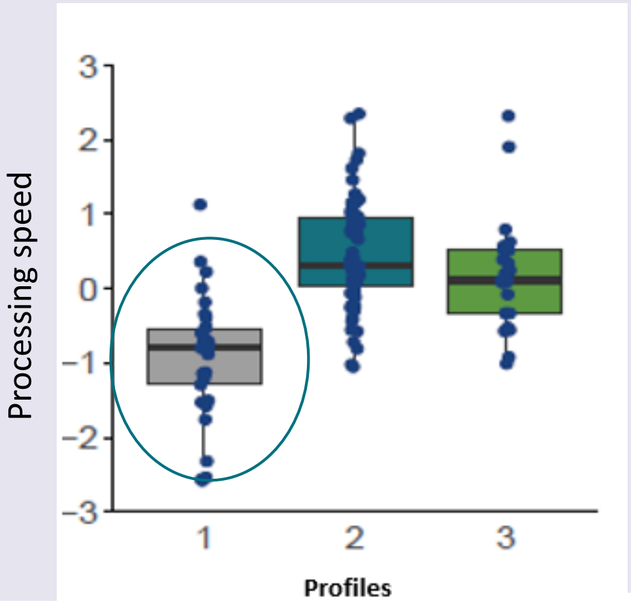
Baseline evaluation - Primary outcomes

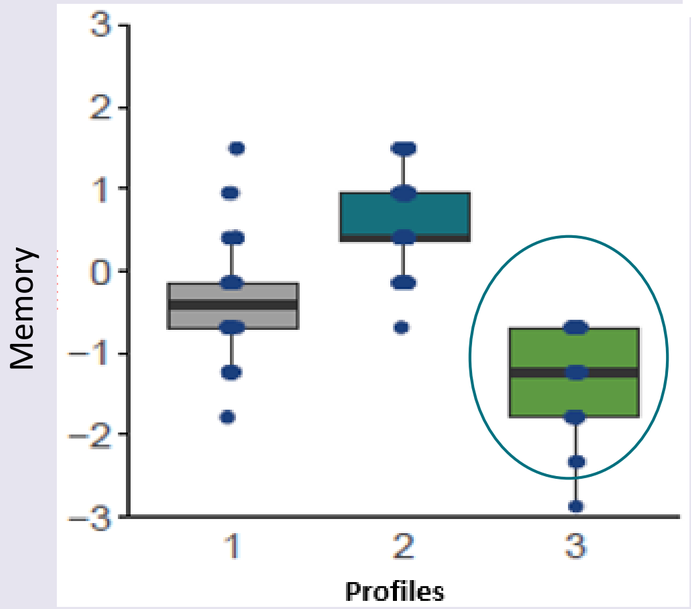
- 40% (N=49) of patients meet the difficulty threshold at the baseline for executive control complaints
- 35% (N=43) of patients were severily dissatisfied about their memory functioning at baseline
- No difference observed between groups prior to the interventions (all ps>0.124)

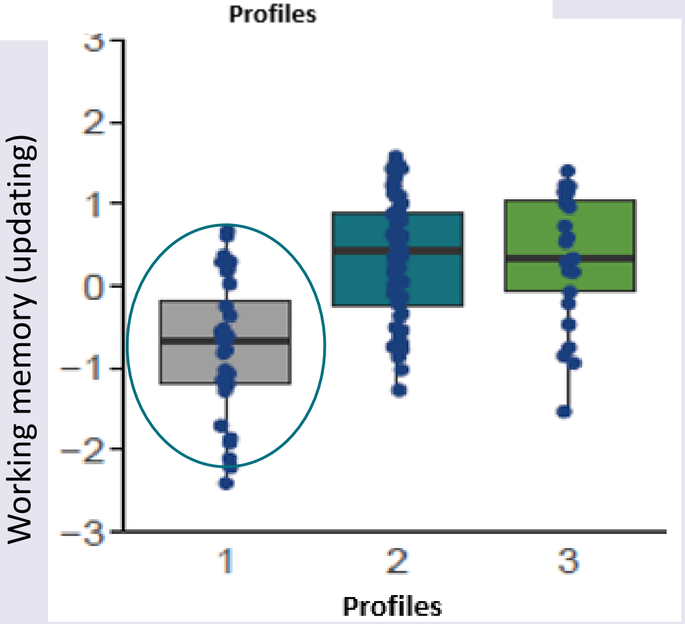
Results

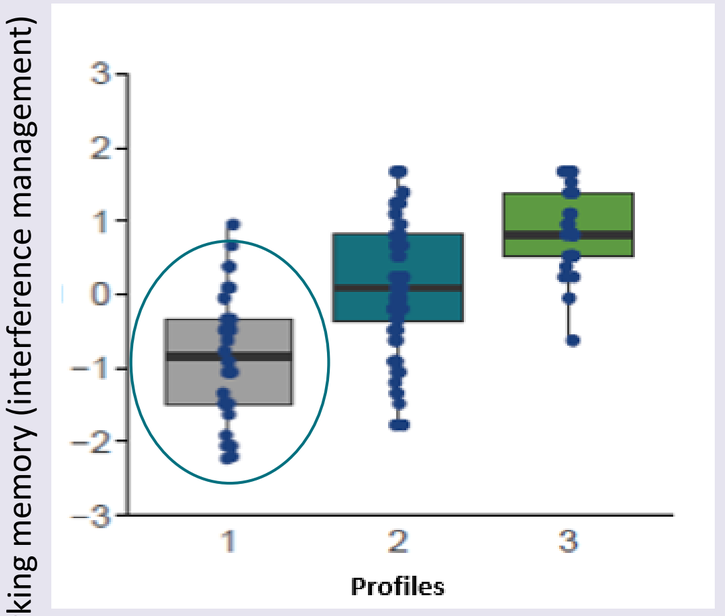
Baseline evaluation – Different cognitive profiles





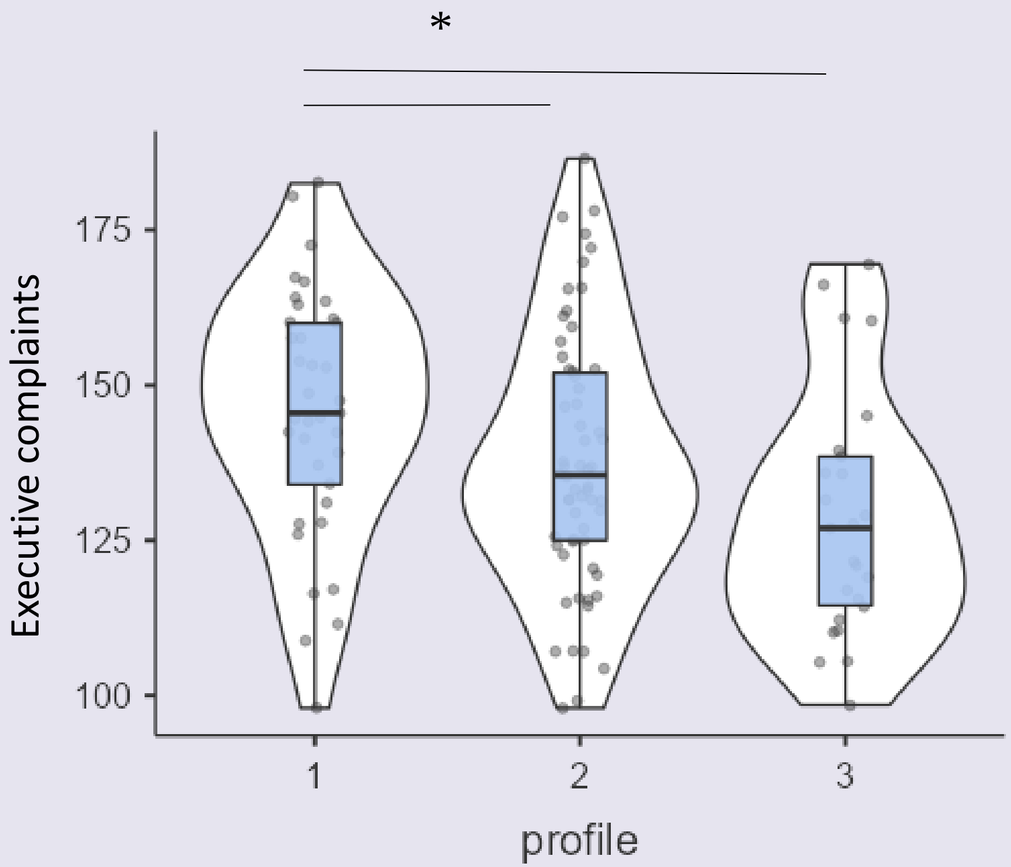




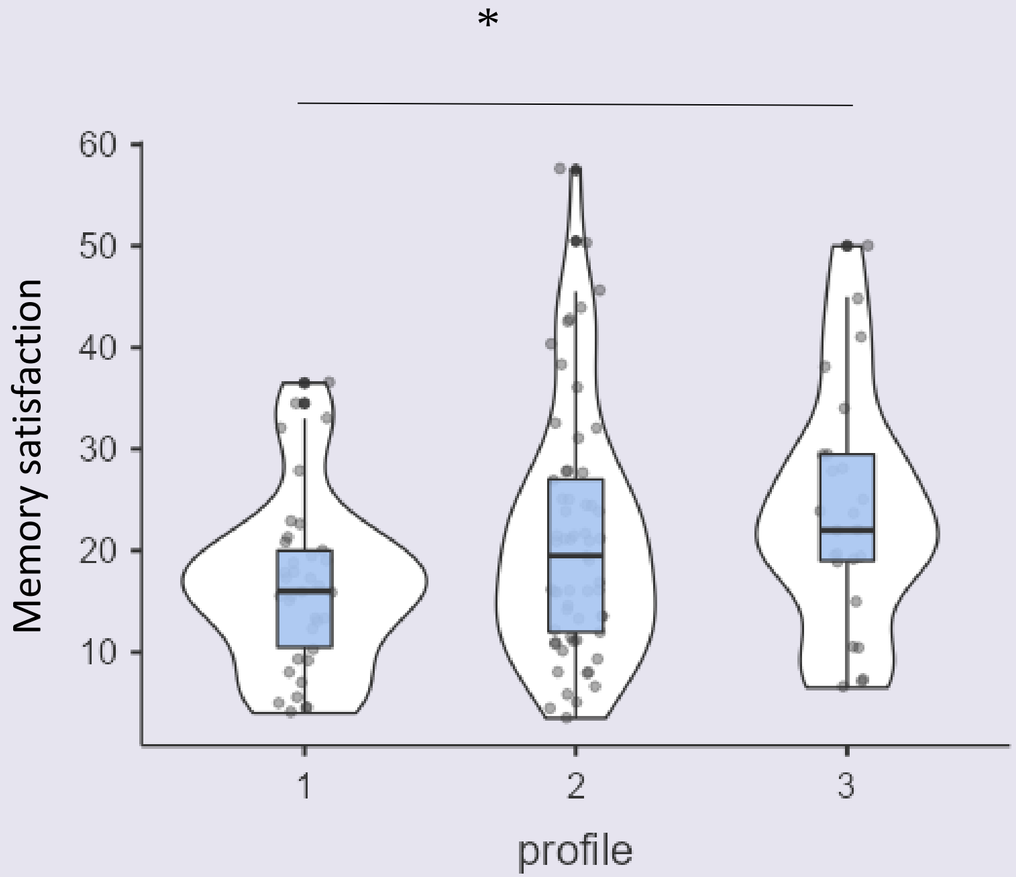


LPA (Latent Profile Analysis); All *ps*<.001

Baseline evaluation – Different cognitive profiles



p=.002



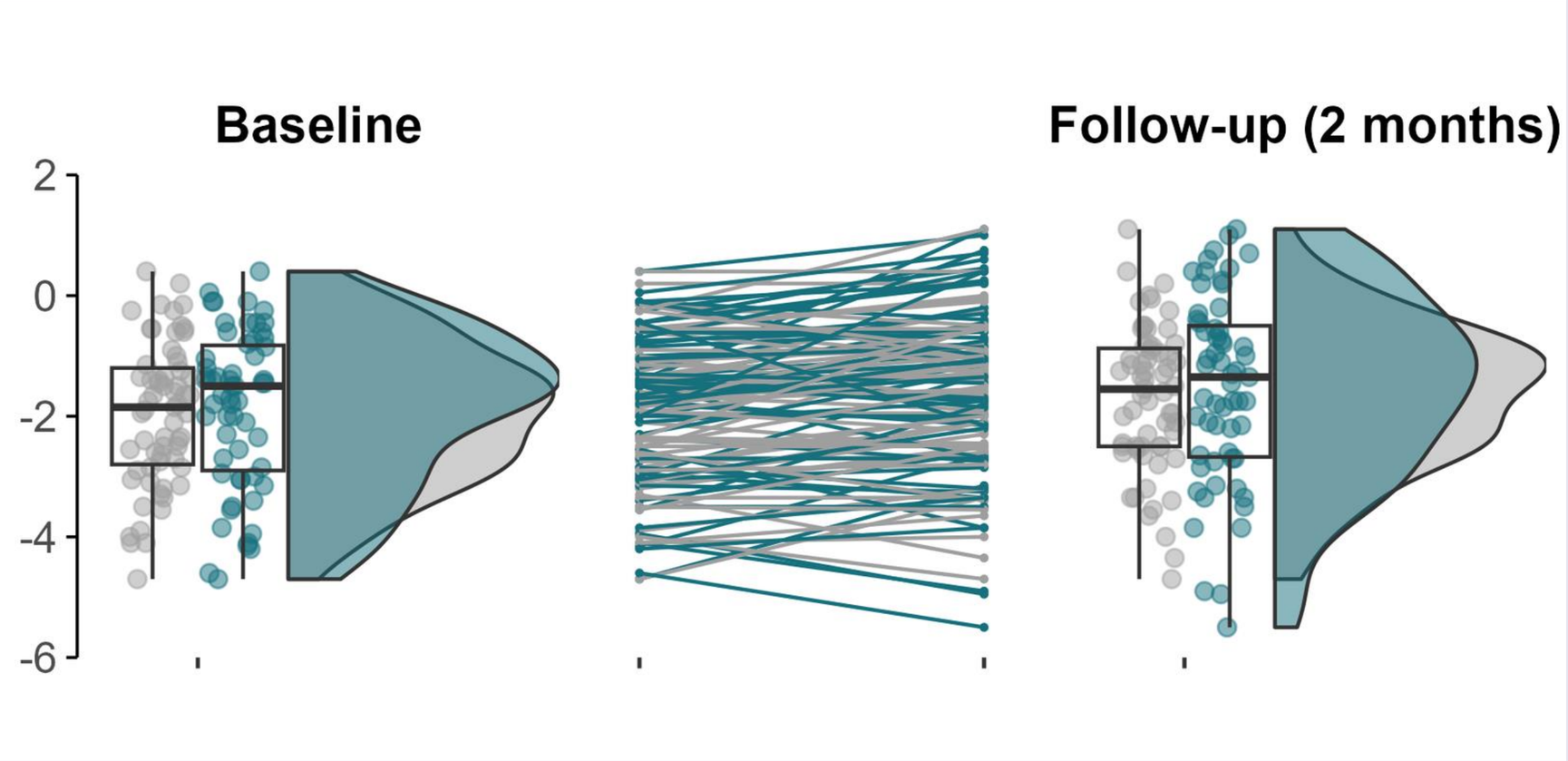
p=.013

Results

2 months follow-up : executive control

less complaints

more complaints



interventions

cognitive

affective

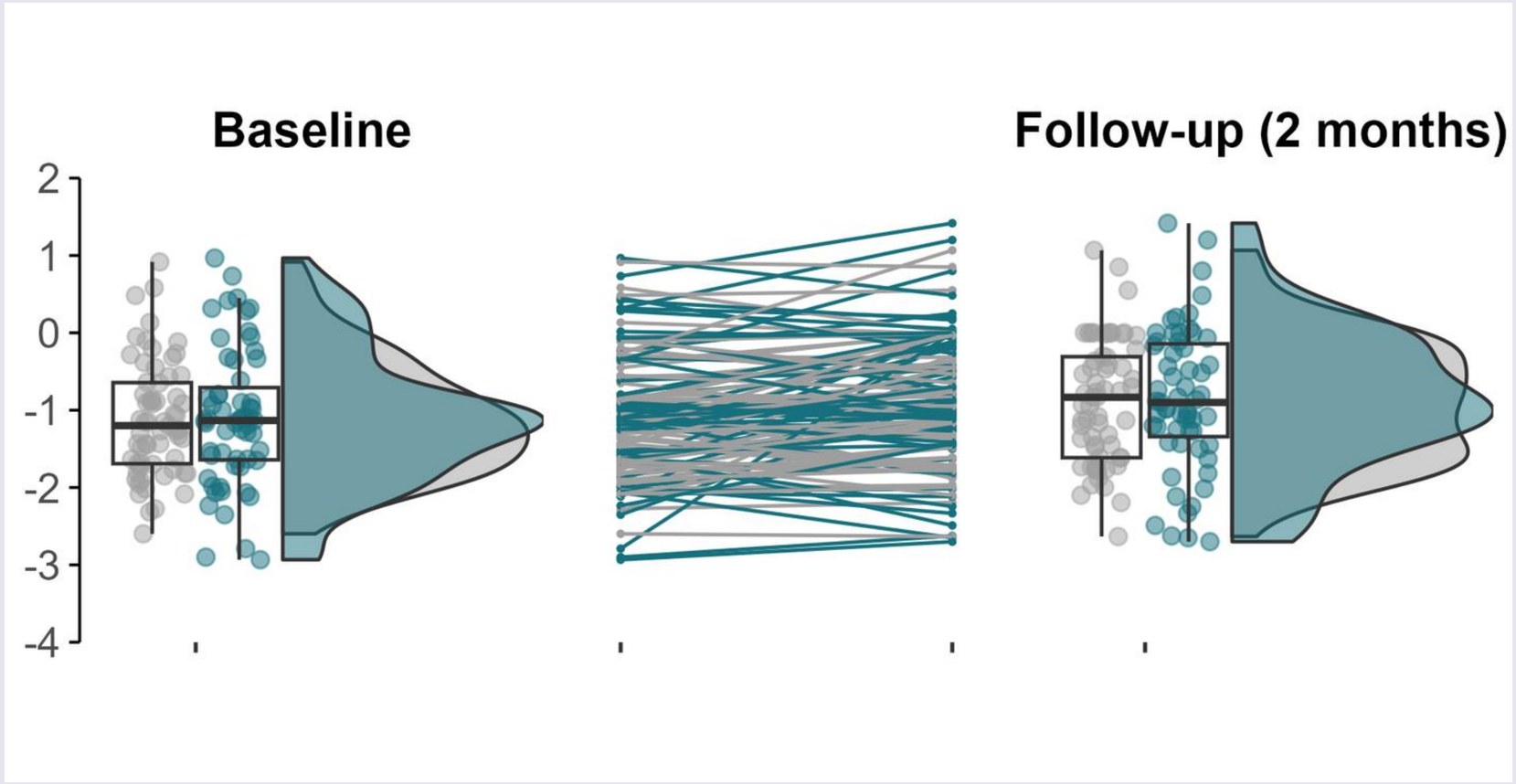
- Executive control complaints decreased at 2 months FU for both intervention groups (*F* = 17.417, p = .008, SES = -0.14 [95% CI: -0.21, -0.07])
- No moment*group interaction (*F* = 0.173 ; *p*=0.67)

Results

2 months follow-up: satisfaction with memory

less complaints

more complaints



interventions

cognitive

affective

- Memory complaints decreased at 2 months FU for both intervention groups, (F = 16.325 ; p<.001, SES = -0.11 [95% CI: -0.16, -0.06])
- No moment*group interaction effect (F=0.034 ; p=0.8)

Results

2 months follow-up: secondary outcomes

	Time effect on secondary outcomes			
	F value	**P value**	**SES**	**95% IC**
Cognitive Tests				
Attention	9.861	**.002**	-0.15	[-0.24, -0.06]
Memory	10.218	**.002**	-0.13	[-0.21, -0.05]
Executive	3.742	.055	-0.09	[-0.18, 0.00]
Quality of Life	12.873	**<.001**	0.16	[0.07, 0.24]
Fatigue				
Physical Fatigue	13.304	**<.001**	0.15	[0.07, 0.23]
Cognitive Fatigue	20.630	**<.001**	0.22	[0.12, 0.32]
Psychosocial Fatigue	2.8315	.09	0.08	[-0.01, 0.18]
Sleep	5.4345	**.02**	0.10	[0.01, 0.18]
Psychological distress	3.5096	.06	0.07	[0.00, 0.15]
Activities				
activity_impairment	3.289	.07	0.07	[-0.01, 0.15]
work_impairment	7.578	**.007**	0.13	[0.04, 0.22]

Influence of sponteneous recovery ?

Linear regressions :

- No time effect between first infection and baseline evaluation (cognitive control, p=0.77; memory, p=0.64)
- No time effect between first infection and follow-up evaluation (cognitive control, p=0.69; memory, p=0.15)

Sponteneous recovery is highly unlikely

Conclusions and perspectives

- For both intervention groups : decrease in cognitive complaints; attentional and memory domains; quality of life; fatigue and sleep difficulties; and impairment on work

- Significant improvement due to specific aspects of the interventions ? general effect ? placebo response ?

In perspective :

- Specific benefits of one or the other intervention on certain outcomes ?
- Trajectory analysis

Trajectoire Covid-Long

Cette convention est disponible jusqu'au 31 décembre 2025.

Kinésithérapie :

- 60 séances individuelles de kinésithérapie (30 min).

(ex. exercices de respiration ; stimulation physique modérée et structurée)

Diététique :

- 7 séances individuelles en diététique. Examen diététique.

Ergothérapie :

- 14 séances individuelles. Examen de capacités et limitations fonctionnelles, aménagement.

Neuropsychologie :

Examen cognitif et 10 séances individuelles de prise en charge.

Thank you very much!