MAYO CLINIC

MEETING OF THE COMMITTEE ON EXAMINING THE WORKING DEFINITION FOR LONG COVID

LONG COVID DEFINITION CONSIDERATIONS

Ryan T. Hurt, MD, PhD
Ravindra Ganesh MBBS, MD

January 18, 2024

TERMINOLOGY AND TIMING

- Long COVID is most appropriate name given predominant use in media/social media
- Defining point should be from onset of symptoms of index infection

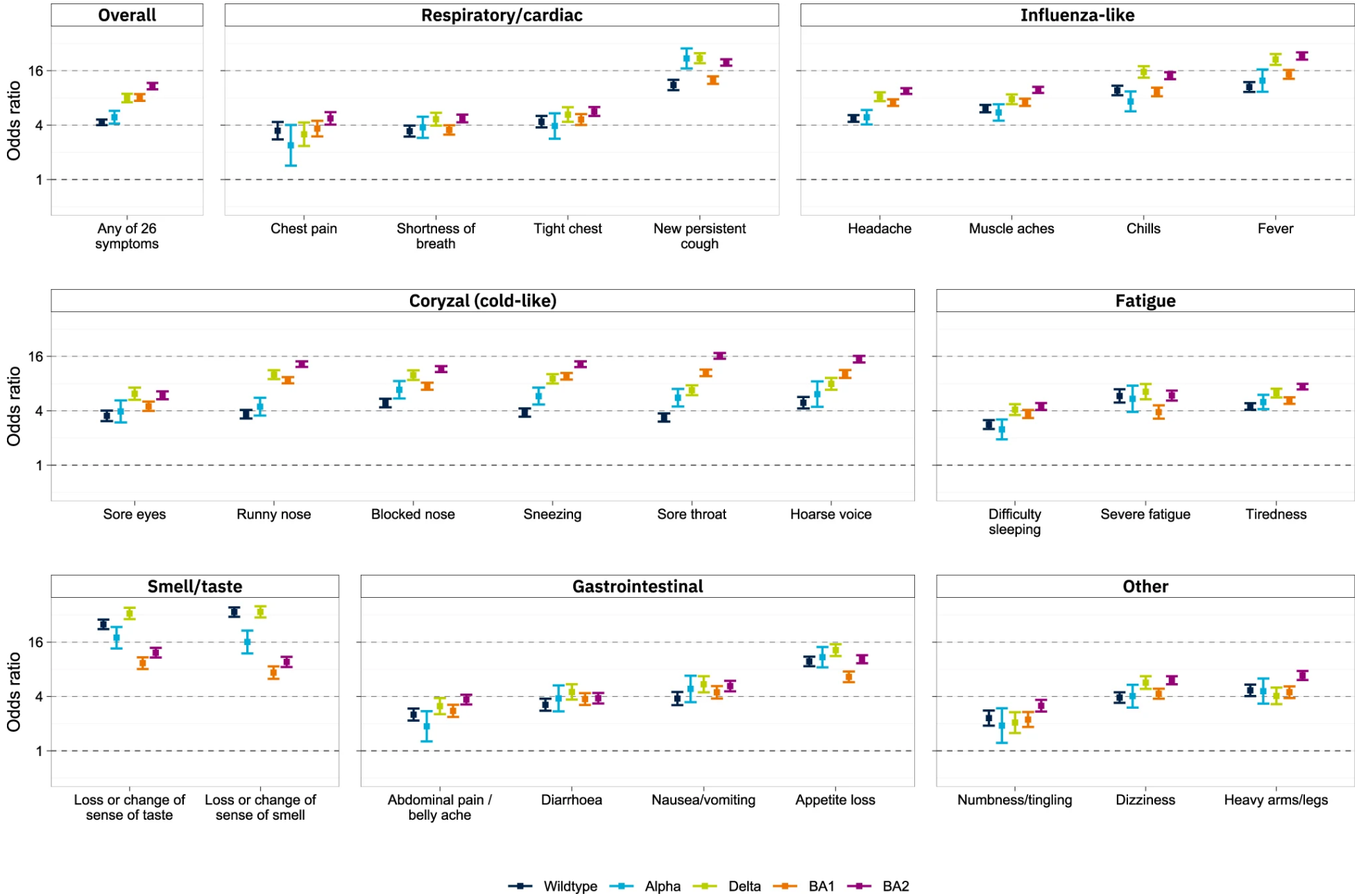
TIMING

Criteria	Institution					
	Mayo Clinic	NIH	CDC	NHS	WHO	Derivative
Testing necessary	No	No	No	No	No	No
Time after initial infection, days	≥21	Not listed	≥28	≥84	≥60	≥28
Not better explained by an alternative diagnosis	Yes	No	No	Yes	Ye	Yes
Lists common symptoms	Yes	No	No	Yes	Yes	Yes
Decreased functioning as criterion	No	No	Yes	Yes	Yes	Yes

Long COVID | NIH COVID-19 Research
Long COVID or Post-COVID Conditions | CDC
Long-term effects of COVID-19 (long COVID) - NHS (www.nhs.uk)
Post COVID-19 condition (Long COVID) (who.int)
Mueller MR et al, Post COVID Conditions, Mayo Clin Proc. July 2023;98(7):1071-1078

SYMPTOMS

- Should include both persistent and new symptoms.
- Symptoms may fluctuate over the course of illness.
- Patients may have a brief asymptomatic phase before symptoms re-emerge for Long COVID symptoms



Whitaker, M., Elliott, J., Bodinier, B. *et al.* Variant-specific symptoms of COVID-19 in a study of 1,542,510 adults in England. *Nat Commun* **13**, 6856 (2022).

- 536 respondents Post COVID Care Clinic (725 surveyed; 74% response)
- Mean age 52.3 years (sd = 14.1)
- Female 63%
- Mean time since first positive test 23.3 months (sd = 6.4)
- At follow up only 4.5% (24/536) were fully recovered

Symptom	Baseline (N=536†)	Follow-up (N=536†)	Signed Rank p-value
Overall level of functioning	8 (6, 9)	5 (3, 8)	<0.001
Individual symptoms			
Fatigue	8 (7, 10)	6 (3, 8)	<0.001
Brain fog	8 (6, 9)	5 (3, 8)	<0.001
Shortness of breath	6 (3, 8)	3 (1, 6)	<0.001
Muscle pain	6 (2, 8)	3 (1, 6)	<0.001
Headache	6 (2, 8)	3 (1, 6)	<0.001
Rapid heart rate/Light-headedness with standing	6 (2, 8)	3 (1, 5)	<0.001
Insomnia	6 (1, 8)	3 (1, 7)	<0.001
Dizziness	5 (1, 8)	2 (1, 5)	<0.001
Balance difficulties	4 (1, 7)	2 (1, 5)	<0.001
Chest Pain	3 (1, 6)	1 (1, 4)	<0.001
Tinnitus	1 (1, 6)	1 (1, 5)	<0.001

Table 2. Overall Level of Functioning and Symptom Severity at Baseline and Follow-up*

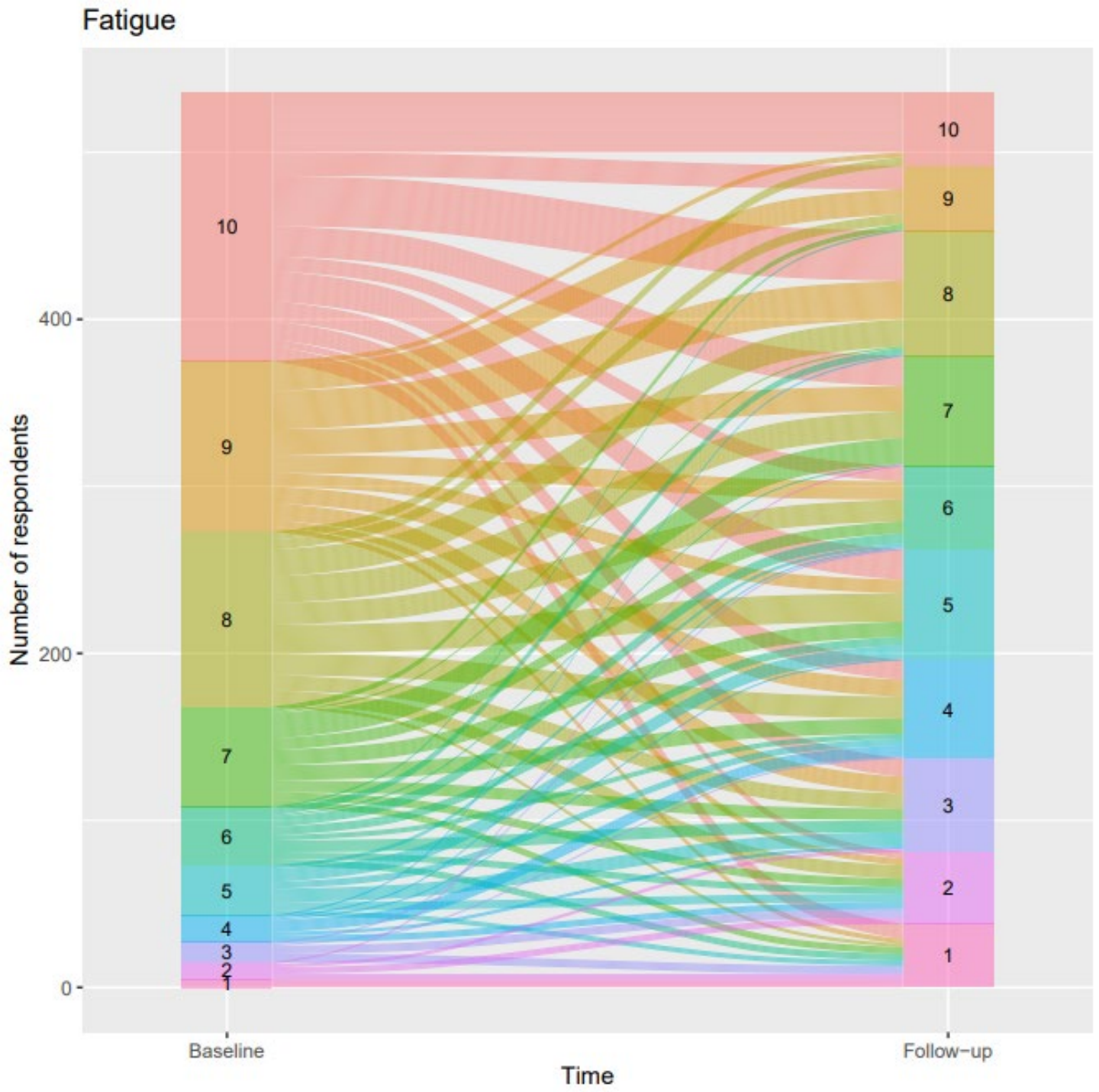
***Patients were asked to rate the severity of each symptom on a scale from 1 to 10 where 1 corresponded to "not significant" and 10 corresponded to "extremely significant". Data are summarized by presenting the median (25th, 75th) and compared between time periods using the signed rank test.**

†Due to missing data, the number of respondents included for a given symptom ranged from 533 to 536.

Post COVID Care Clinic – unpublished data

SYMPTOM TRAJECTORY

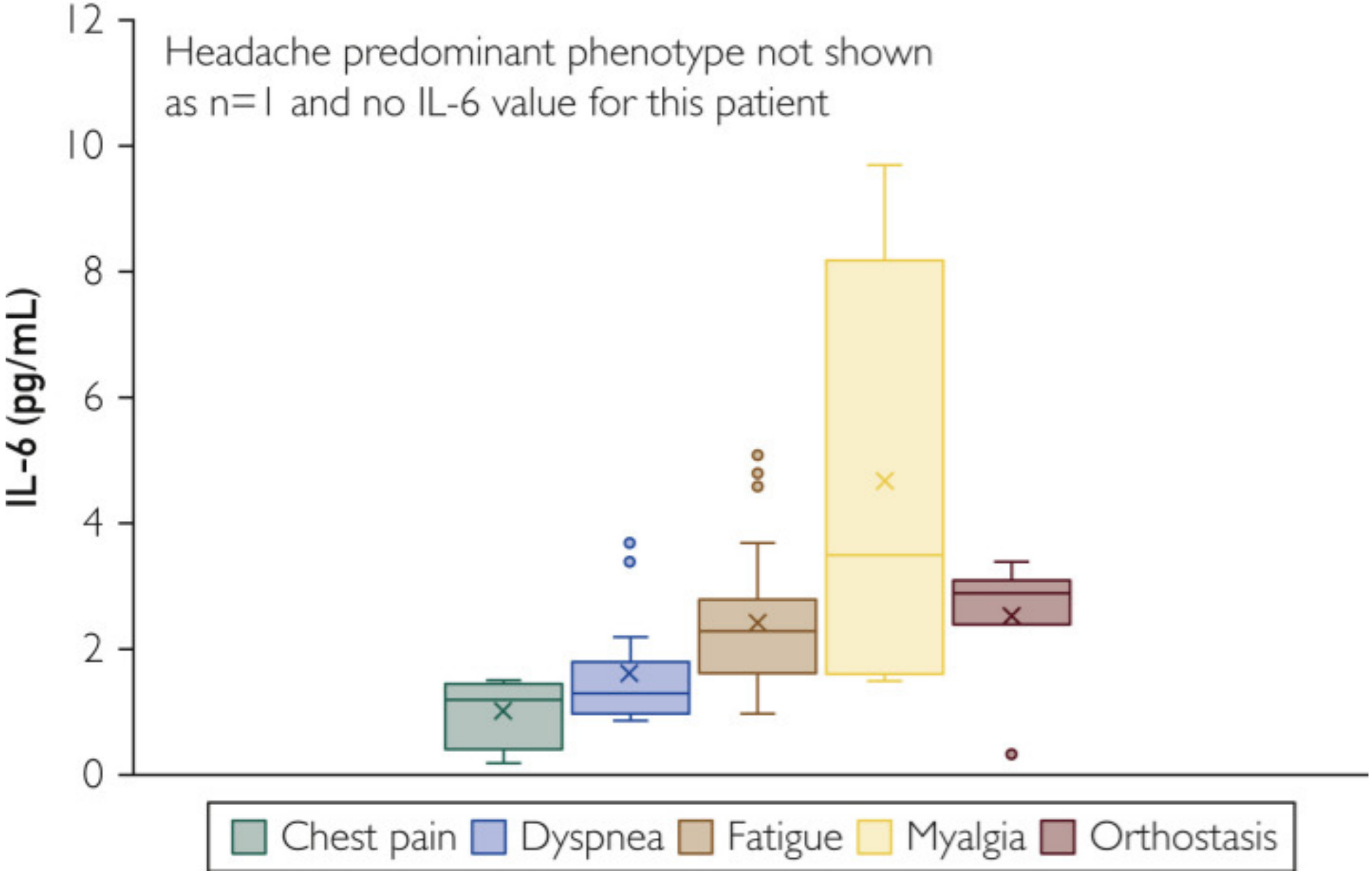
- Bidirectional
- Significant trend towards improvement



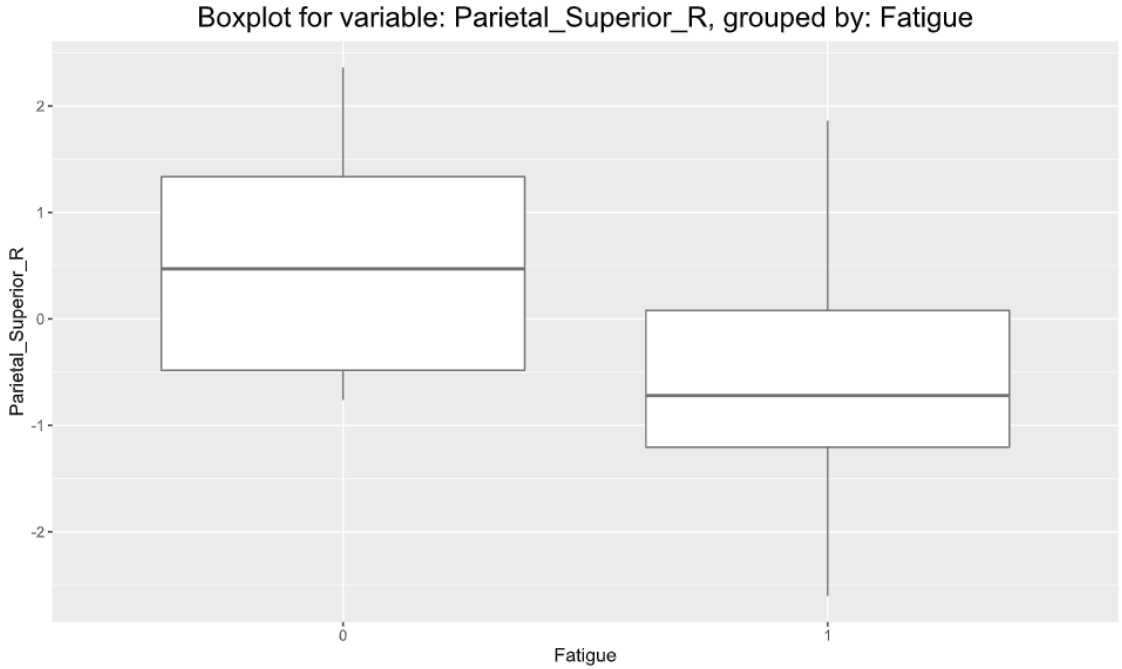
Post COVID Care Clinic – unpublished data

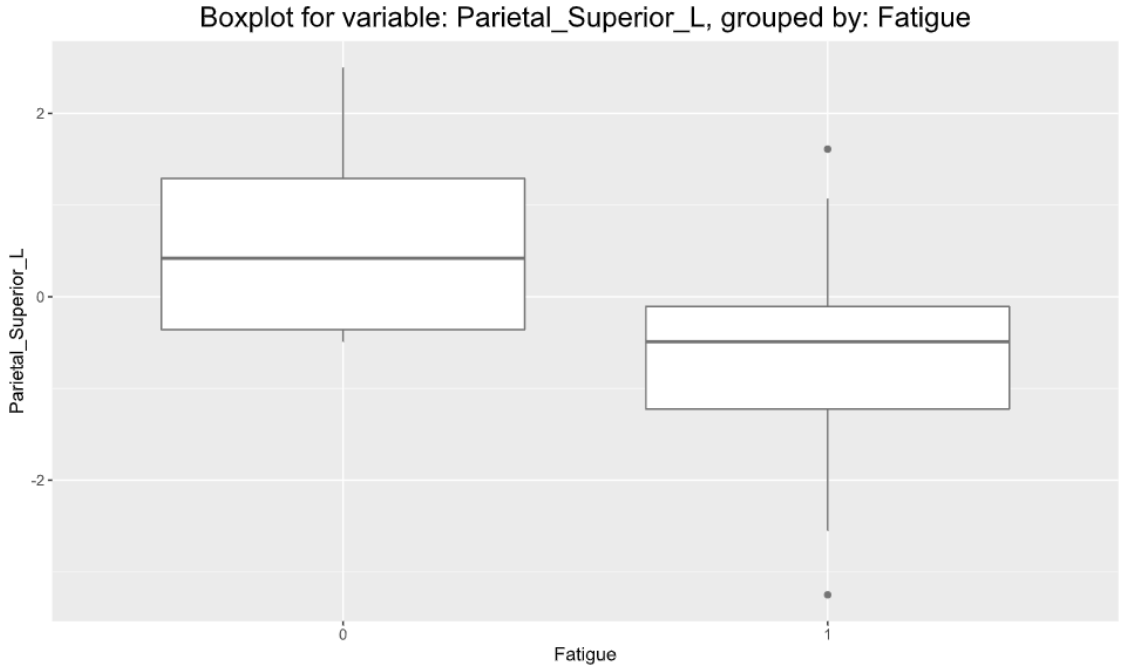
PHENOTYPING APPROACH

- Divergence in outcome trajectory between those with fatigue and post-exertional malaise and those without.
- We phenotype to predominant features that match previously described syndromes
  - ME/CFS
  - Fibromyalgia
  - Paresthesia/Small fiber neuropathy
  - Dysautonomia/POTS
  - Chronic headache syndromes
- Phenotyping drives treatment



Ganesh et al, *Mayo Clin Proc.* 2022 Mar;97(3):454-464. doi: 10.1016/j.mayocp.2021.11.033.



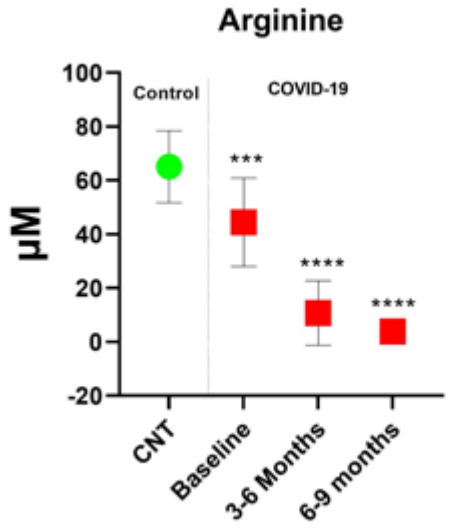


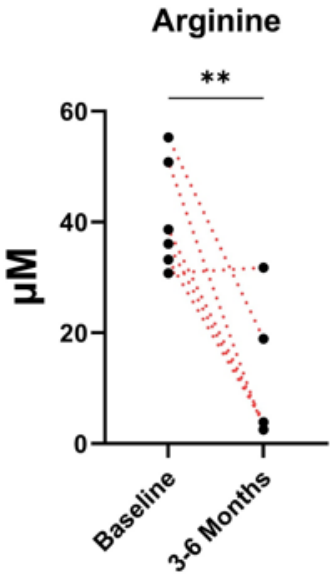
BRAIN PET

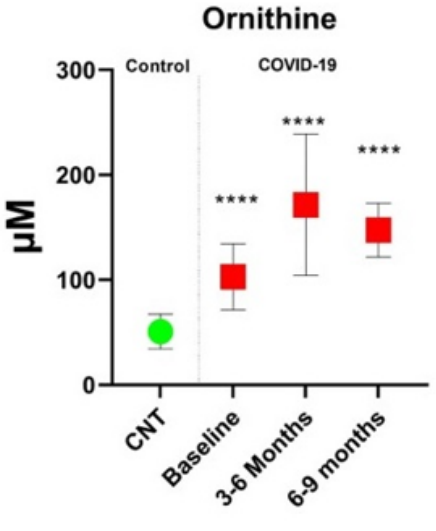
- Patients with LC-fatigue more hypometabolic in multiple brain regions than LC-nonfatigued

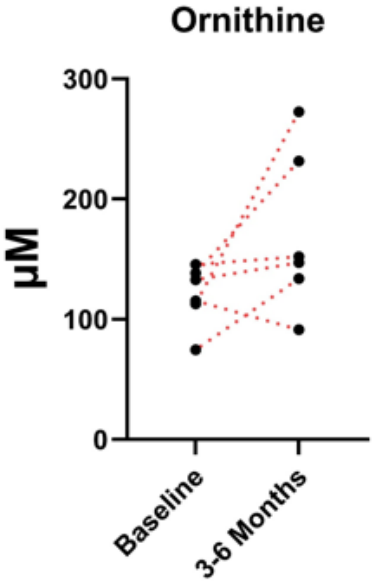
Post COVID Care Clinic – unpublished data

ARGININE & ORNITHINE LEVELS IN LC-FATIGUE









Post COVID Care Clinic – unpublished data

nature communications

Article

https://doi.org/10.1038/s41467-023-44432-3

Muscle abnormalities worsen after post-exertional malaise in long COVID

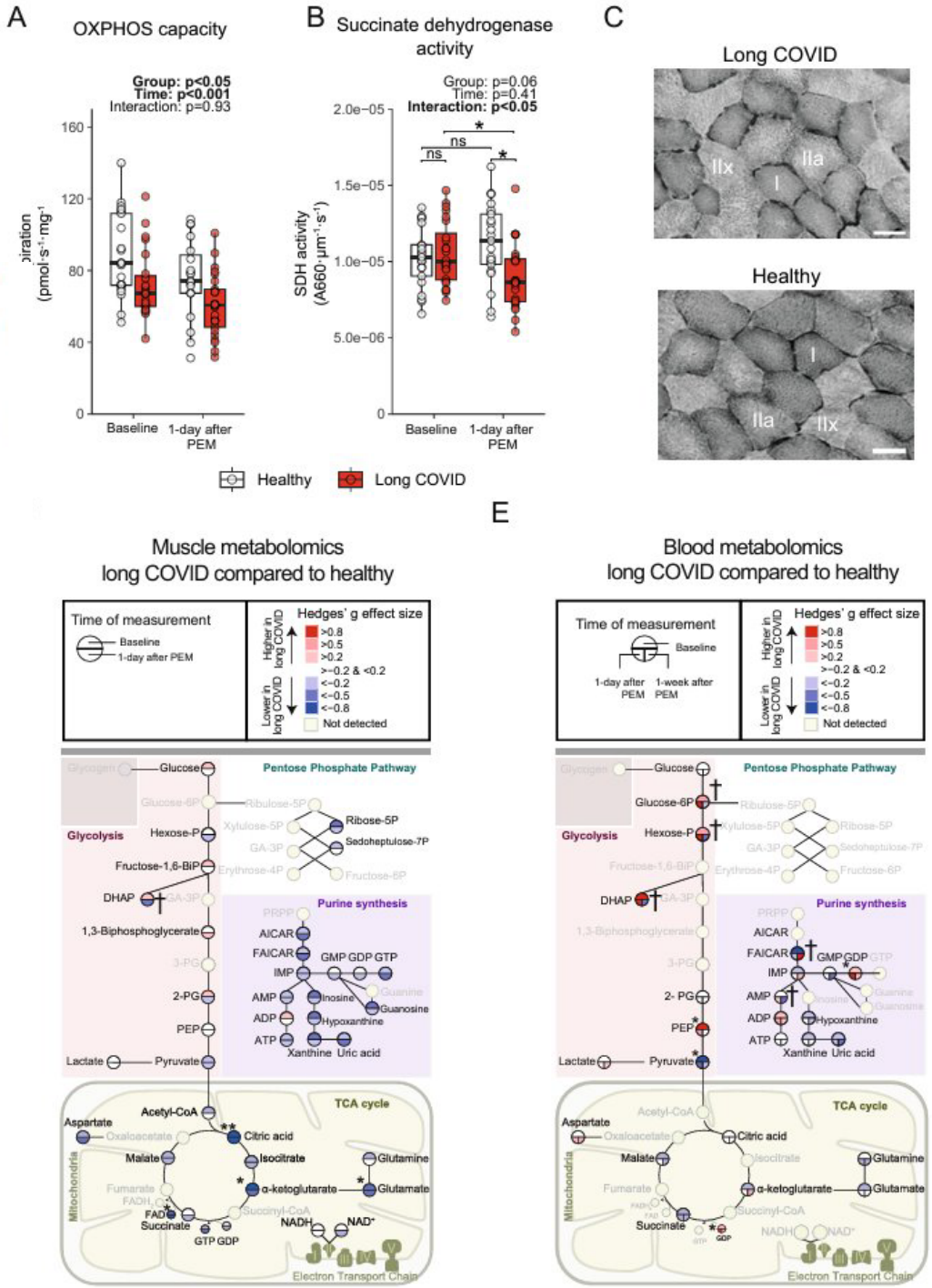
Received: 21 March 2023

Accepted: 13 December 2023

Published online: 04 January 2024

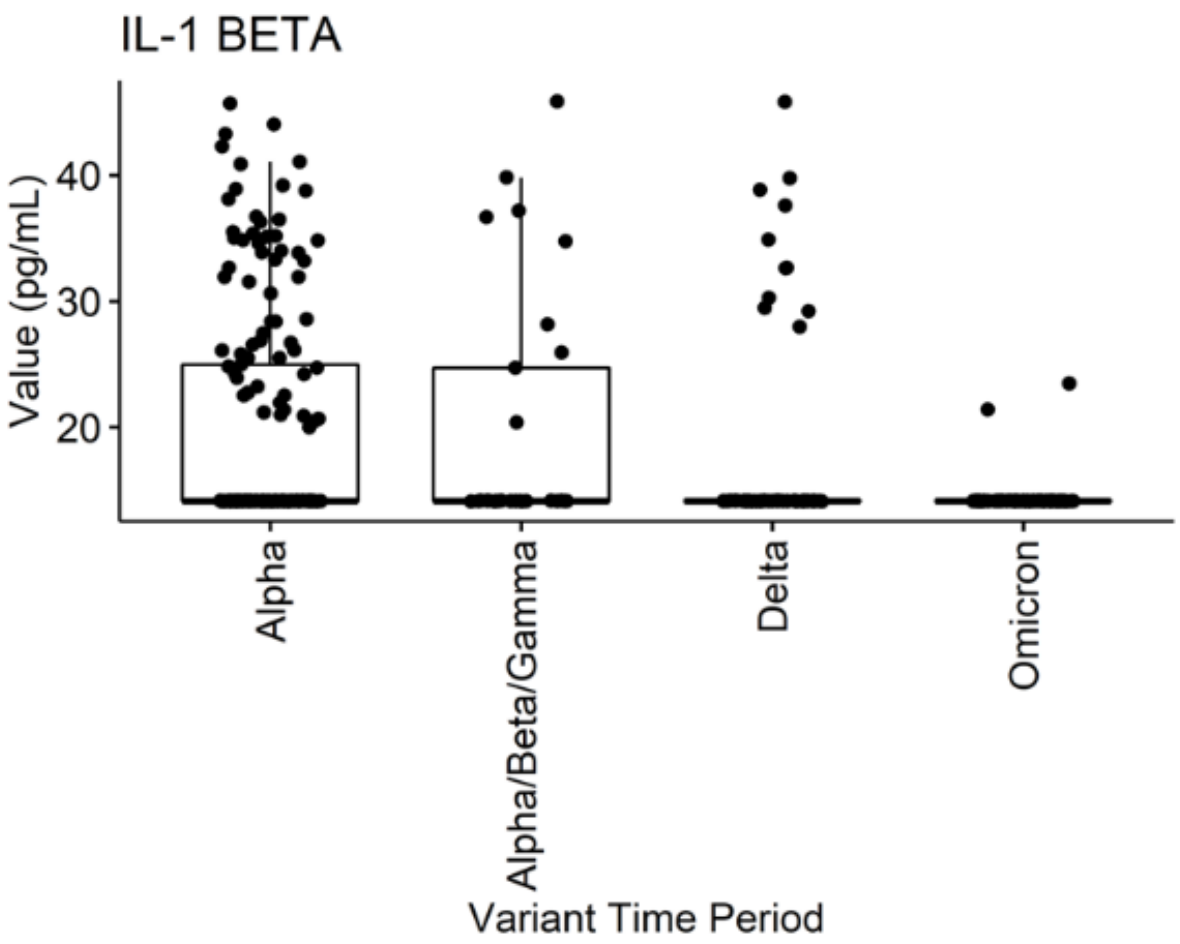
Check for updates

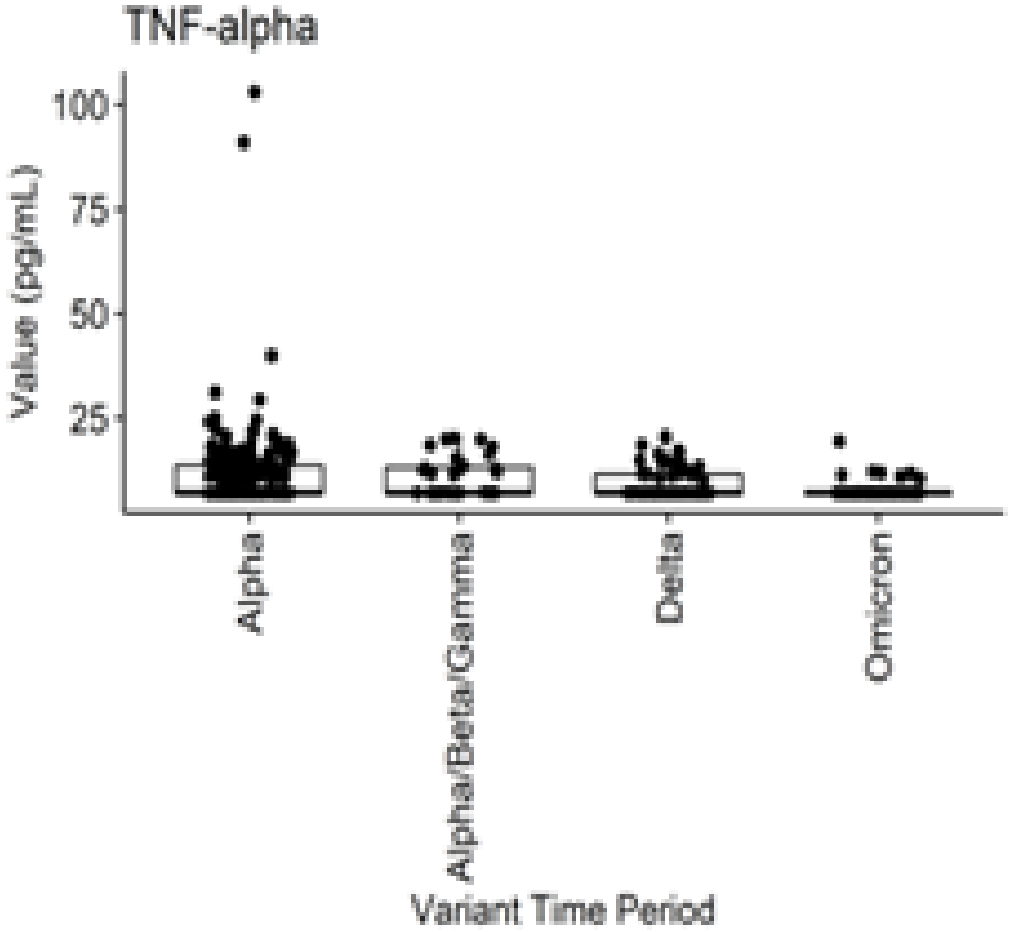
Brent Appelman[1,2,15], Braeden T. Charlton[3,4,15], Richie P. Goulding[3,4], Tom J. Kerkhoff[3,4,5,6], Ellen A. Breedveld[3,4], Wendy Noort[3,4], Carla Offringa[3,4], Frank W. Bloemers[4,7], Michel van Weeghel[8], Bauke V. Schomakers[8], Pedro Coelho[9,10,11], Jelle J. Posthuma[7,12], Eleonora Aronica[11], W. Joost Wiersinga[1,2,13], Michèle van Vugt[2,14,15] & Rob C. I. Wüst[3,4,15]



BIOMARKERS

- No biomarkers reliable in Long COVID
- Prior papers suggested triad of IL-6, IFN-1β and TNF-α
  - This has largely gone away with Omicron
  - Unpublished data





Post COVID Care Clinic – unpublished data

SEVERITY AND IMPAIRMENT

- Wide spectrum of severity
- There is a group of patients with subclinical long COVID who should meet criteria but may not seek medical attention.

THANK YOU