

Vaccination after developing long COVID : impact on clinical symptoms, inflammatory markers and viral persistence

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Conflict Disclosures

I have the following conflicts to declare:

Advisory Board (or equivalent):

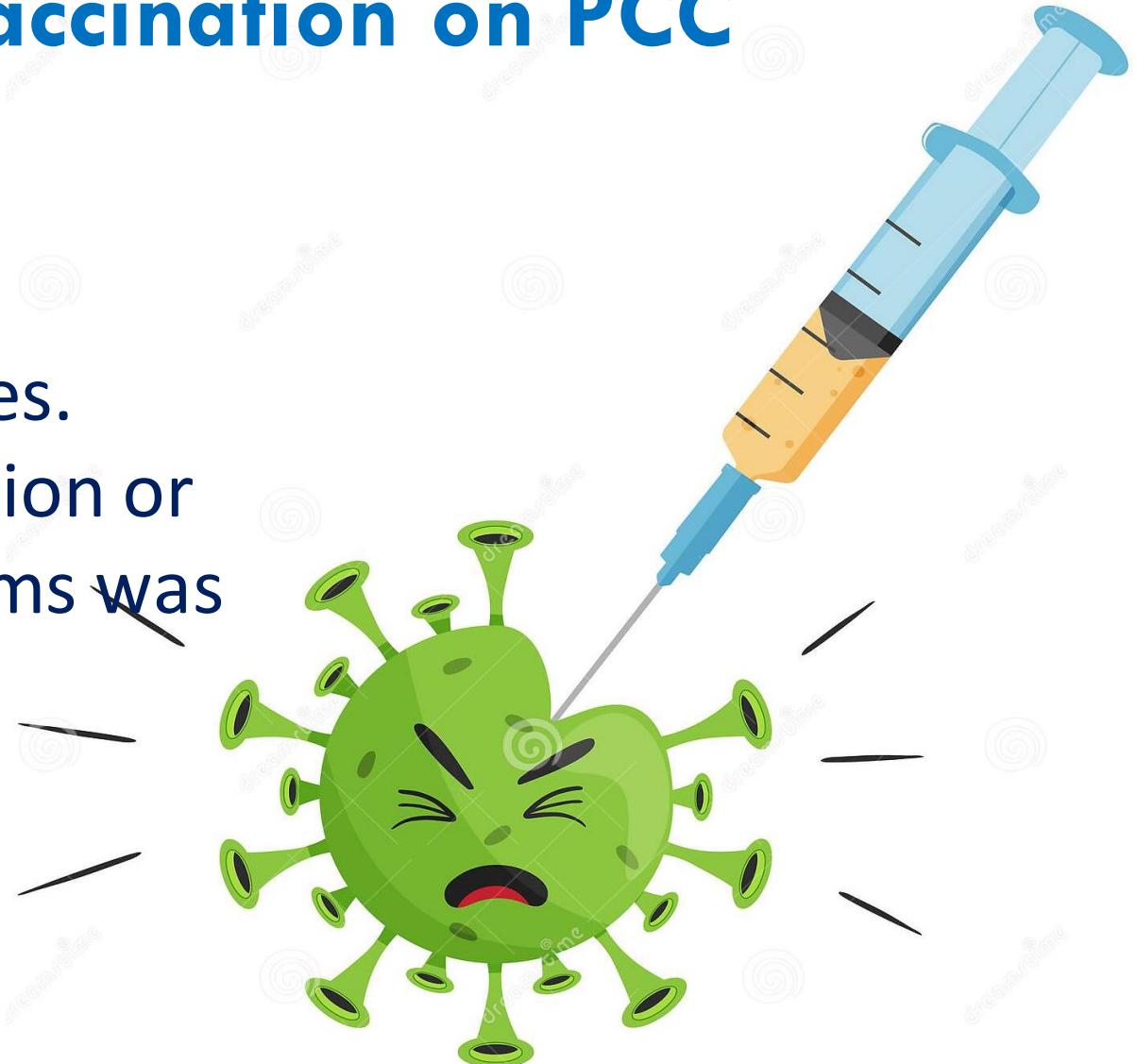
- Long COVID Advisory Board, *Institut National d'Excellence en Santé et en Services Sociaux* (INESSS)
- Subject Matter Expert, Chief Science Advisor Task Force on Post-COVID-19 Condition
- Subject Matter Expert, Post-COVID-19 Condition Round Tables, CIHR and CADTH
- Steering Committee Member, *Biobanque Québécoise de la COVID-19*
- Witness, HESA Committee, House of Commons

Grants or Honoraria:

- | | |
|--|--|
| <ul style="list-style-type: none">• Canadian Institutes of Health Research (CIHR)• <i>Ministère de la Santé et des Services Sociaux</i> (MSSS)• <i>Ministère de l'Économie et de l'Innovation</i> (MEI)• <i>Fonds de Recherche du Québec-Santé</i> (FRQ-S)• COVID-19 Immunity Task Force (CITF)• National Institutes of Health (NIH)• Canada Research Chair• Canada Foundation for Innovation (CFI) | <ul style="list-style-type: none">• Mirella and Lino Saputo Foundation• Fondation J-Louis Lévesque Research Chair• <i>Caisse de dépôt et placement du QC</i>• <i>Fédération des médecins spécialistes du QC</i>• <i>Fédération des médecins omnipraticiens du QC</i>• <i>Tribunal administrative de travail, Gouvernement du QC</i>• <i>Association des pneumologues de la Province de QC</i>• <i>Ordre Professionnel des Inhalothérapeutes du QC</i> |
|--|--|

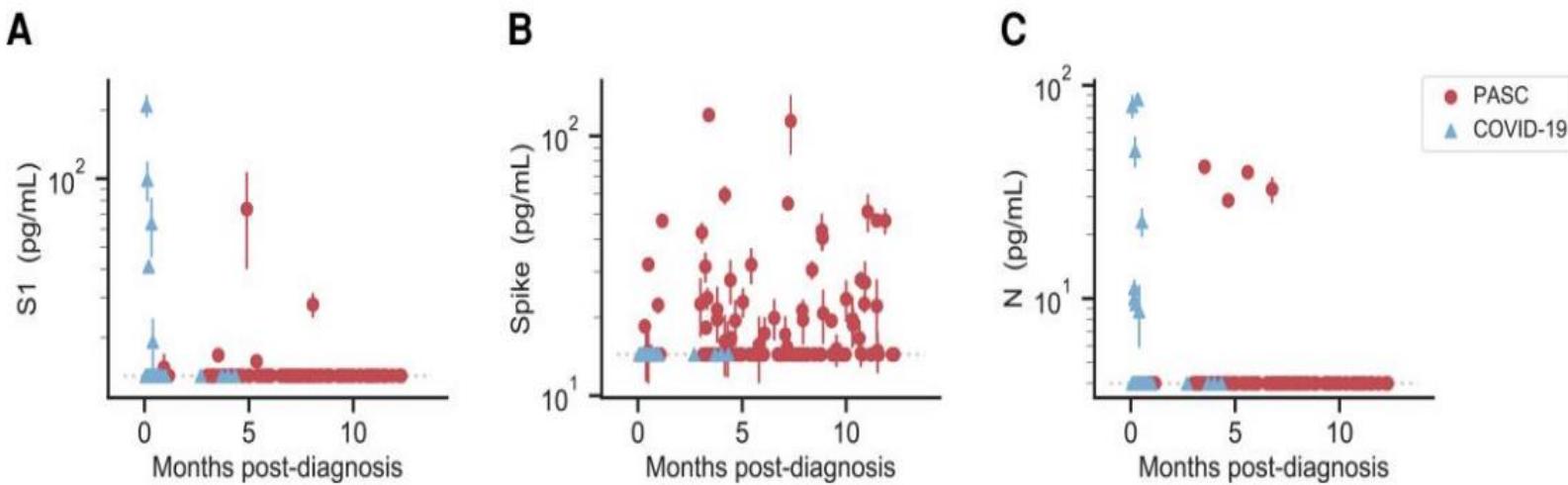
Background - Impact of vaccination on PCC

- Evaluated in at least 10 studies.
- In 7 out of 10 studies, resolution or improvement of PCC symptoms was observed.



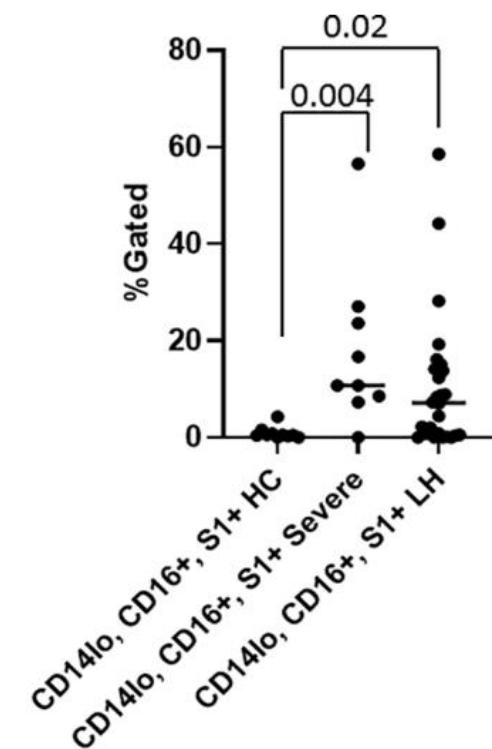
Background - Viral persistence in PCC

SARS-CoV2 antigen levels versus time.



Swank, Z. et al. (2022); Clinical Infectious Diseases.

SARS-CoV2 S1 quantification in non-classical monocytes.



Patterson, B.K. et al. (2022); Frontiers in Immunology.

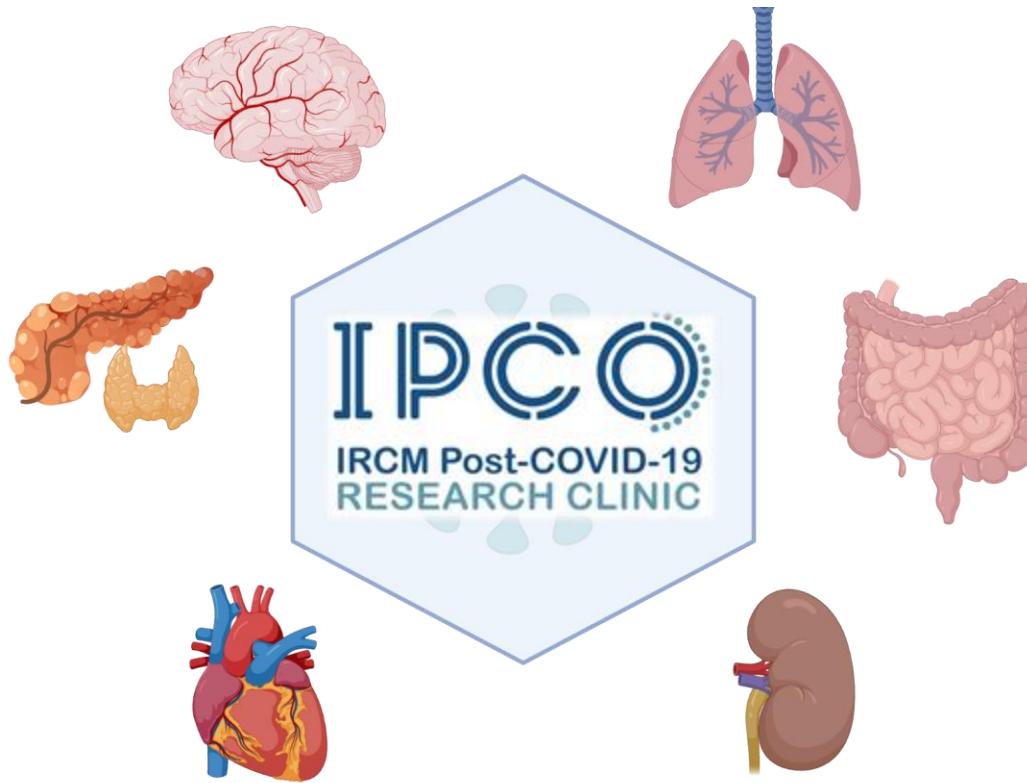
Study Objectives

To determine whether COVID-19 vaccination in patients with post-COVID-19 conditions (PCC) impacts the evolution of :

- Long COVID symptoms and psychological well-being
- Markers of systemic inflammation
- Viral antigen persistence and humoral immune responses

IRCM post-COVID-19 (IPCO) research clinic

Clinicaltrials.gov; NCT 04736732



Integration of clinical care with clinical, translational and fundamental research while establishing a bioresource.

Study schedule



Sub-studies:

1) Impact of COVID-19 vaccine on Long COVID symptoms and immune responses

- Additional visit 2-4 weeks post-vaccination

2) Long COVID and reinfection

- Additional visit at 3 and 6 months post-reinfection

Goal sample size = 500 participants; current n= 263 participants (average of 3 visits per patient)

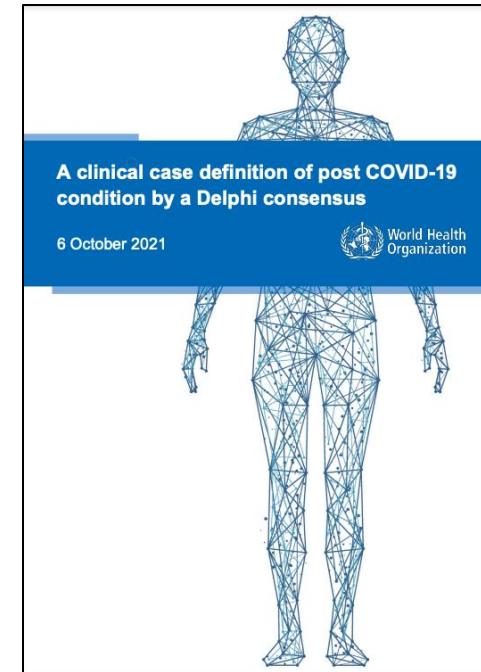
Study procedures

- **Questionnaires and Scores:**
 - Epidemiology
 - Diet questionnaire
 - Well-being index (WHO-5)
 - Frailty score
 - Global health scale
 - Neuropsychiatric testing
- **Medical evaluation:**
 - History and medication (49 symptoms)
 - Vital signs and physical exam
- **Clinical blood and urine tests**
- **Clinically-indicated follow-up testing and referrals**
- **Physiological tests:**
 - BMI and body mass composition
 - Actimetry
 - Continuous blood glucose monitoring
 - Spirometry
 - Cardiac echo
- **Sample collection (biobank) :**
 - NP swab (optional)
 - Saliva
 - Blood (whole blood, PBMCs, serum, plasma)
 - Urine
 - Stool

Inclusion criteria for vaccination in PCC sub-study

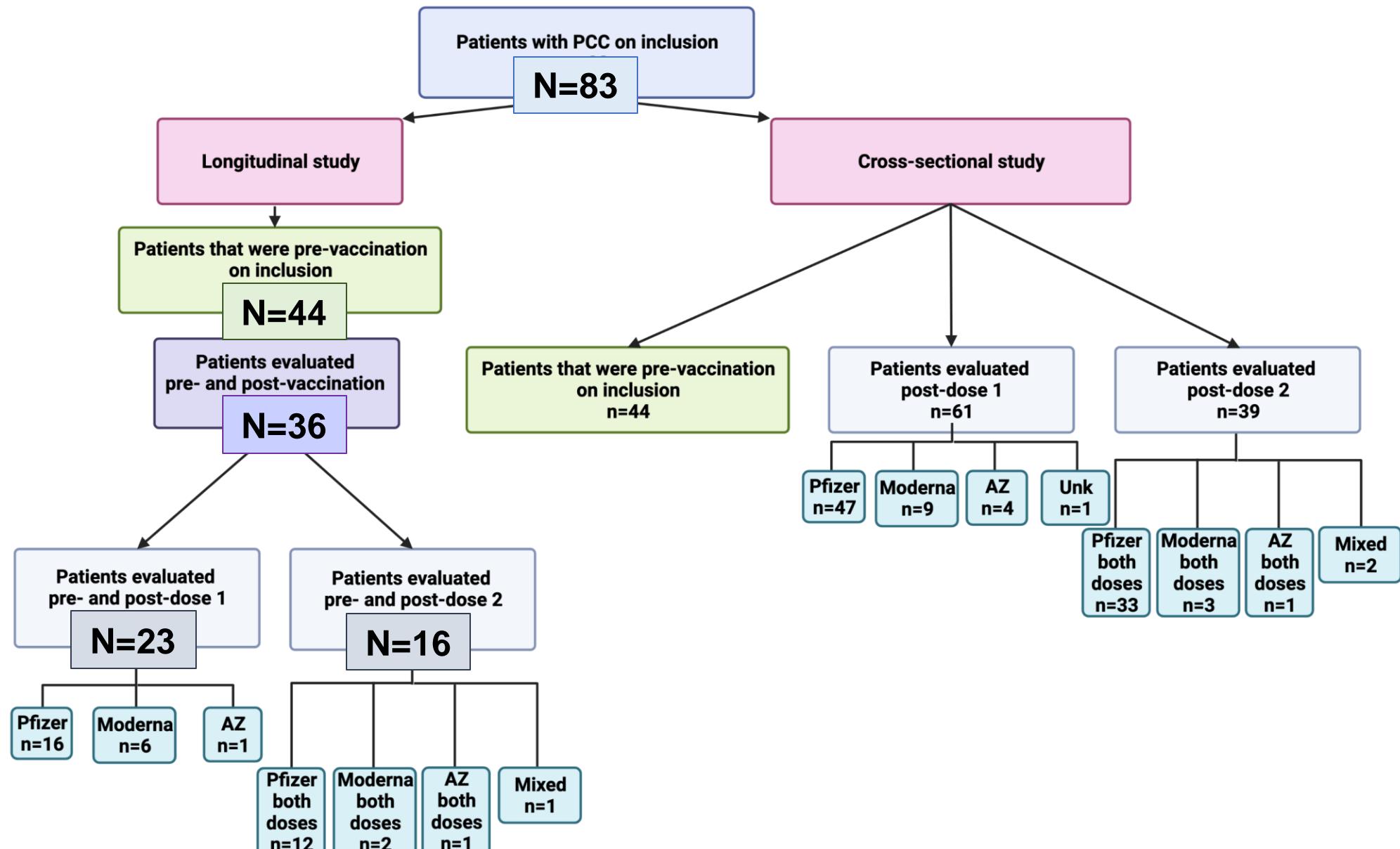
WHO (October 6, 2021)

- Individuals with a history of probable or confirmed SARS-CoV-2 infection.
- 3 months from the onset of COVID-19.
- Symptoms that last for at least 2 months and not explained by an alternative diagnosis.
- Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others which generally have an impact on everyday functioning.
- Symptoms may be of new onset following initial recovery from acute COVID-19, or persist from the initial illness.
- Symptoms may fluctuate or relapse over time.

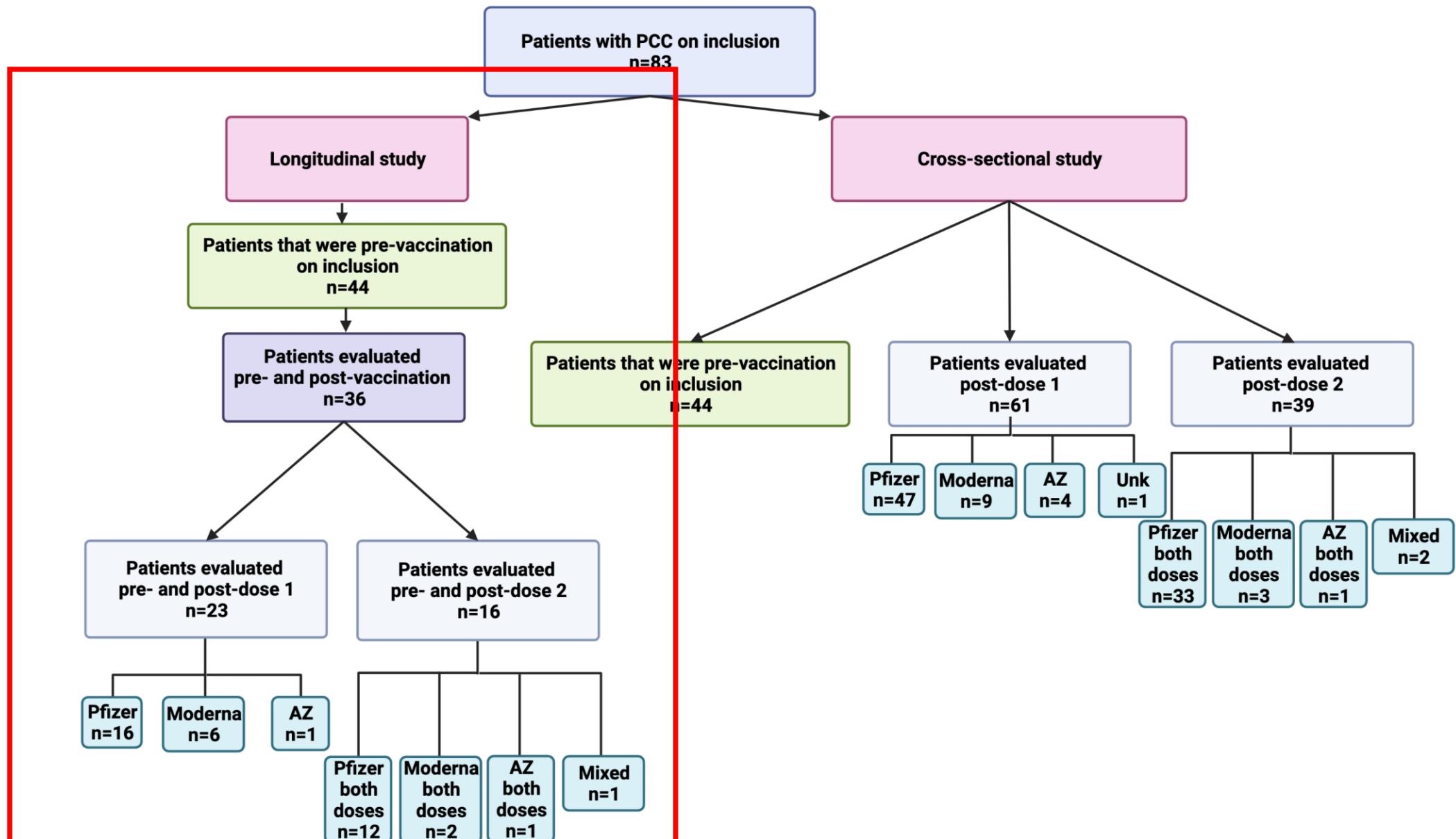


- Participants enrolled in IPCO
- Participants completed a visit between 3 and 6 months post-COVID-19 and met the WHO criteria for PCC at the time of the visit

PCC and Vaccination: Study Design



PCC and Vaccination: Study Design



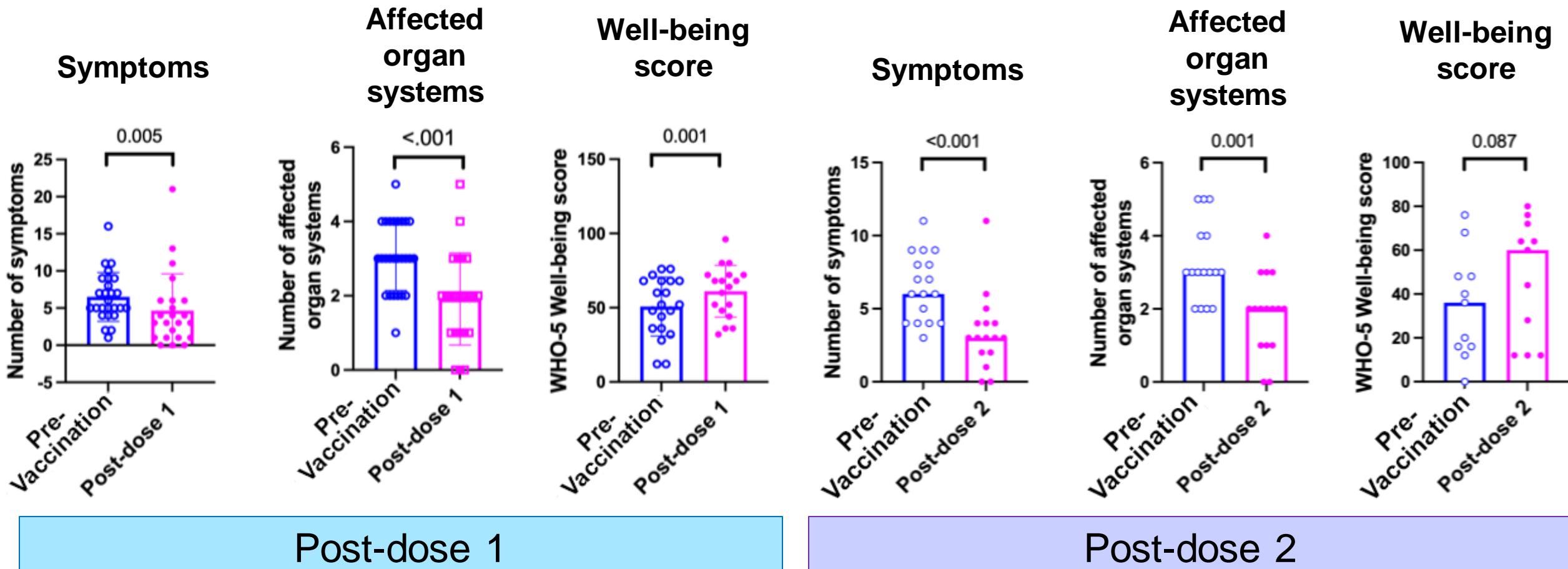
Demographic and Clinical Characteristics

	All participants (n= 83)
Age, mean (SD), years	49.9 (13.6)
Female, n (%)	55 (66.2)
Smoker, n (%)	
Ever	38 (45.8)
At inclusion visit	1 (1.2)
Co-morbidities before COVID-19 diagnosis, n (%)	
Diabetes (Type 1 or 2)	6 (7.2)
Thyroid disorders	11 (13)
Chronic obstructive pulmonary disorder or asthma	7 (8.4)
Sleep apnea	6 (7.2)
Coronary artery disease	1 (1.2)
Dyslipidemia	8 (9.6)
Hypertension	16 (19.2)
Psychiatric disorders	17 (20.4)
BMI at inclusion	
Mean (SD)	25.7 (5.3)
BMI ≥30, n (%)	17 (20.5)
Acute COVID-19 severity, n (%)	
Severe/moderate (WHO 4-9)	11 (13.2)
Number of symptoms during acute COVID-19; mean (SD)	12.5 (4.5)

Impact of vaccination on PCC symptoms and clinical tests (PD1 or 2)

	Pre-vaccination, n=36	Post-vaccination, n=36 (Post-dose 1 or 2)	P value
CBC ¹			
Hg below normal range, n (%)	1 (3.1)	2 (6.3)	1
Total WBC ($10^9/L$; mean (SD))	5.18 (1.15)	5.19 (1.05)	0.92
Lymphocyte count ($10^9/L$; mean (SD))	1.58 (0.43)	1.64 (0.49)	0.38
Platelets ($10^9/L$; mean (SD))	257.63 (45.08)	256.03 (54.39)	0.80
MPV (fL; mean (SD))	8.85 (0.73)	8.73 (0.80)	0.09
Markers of inflammation			
CRP ($>10.0 \text{ mg/L}$; n (%)) ²	0 (0)	0 (0)	NA
D-Dimer ($\mu\text{g/L}$; >600 ; n (%)) ³	2 (8.3)	4 (16.7)	0.50
Ferritin ($\mu\text{g/L}$; mean (SD)) ⁴	81.13 (61.33)	70.37 (49.71)	0.004
Fibrinogen (g/L; mean (SD)) ⁵	3.61 (0.64)	3.48 (0.83)	0.27
≥ 1 ongoing PCC symptom, n (%)	36 (100)	32 (88.9)	NA
Number of PCC symptoms, mean (SD)	6.56 (3.10)	3.92 (4.02)	<0.001
Number of affected organ systems, mean (SD)	3.19 (1.04)	1.89 (1.12)	<0.001
WHO-5 Well-Being Index ⁶			
Mean (SD)	42.67 (22.76)	56.15 (22.83)	<0.001
Score ≤ 50 , n (%)	17 (62.96)	9 (33.33)	0.008

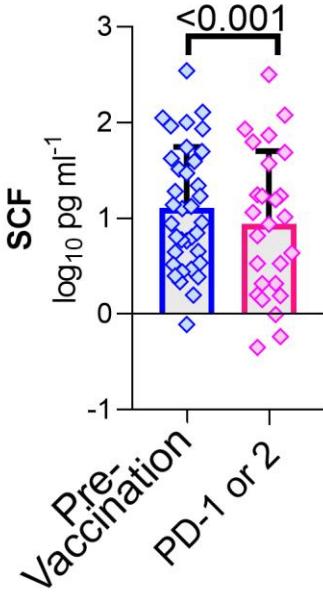
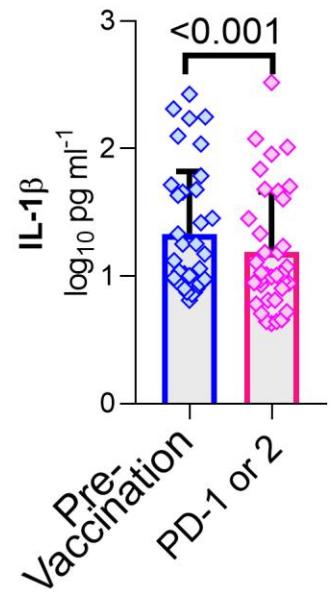
Impact of vaccination on PCC Symptoms



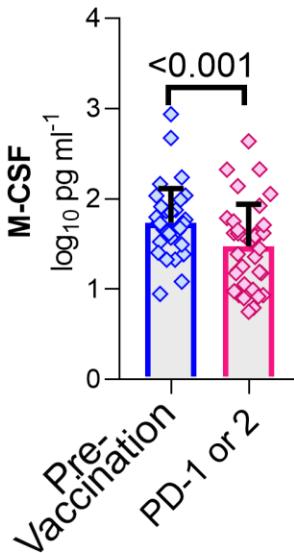
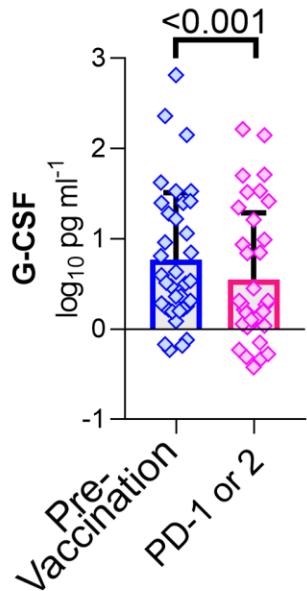
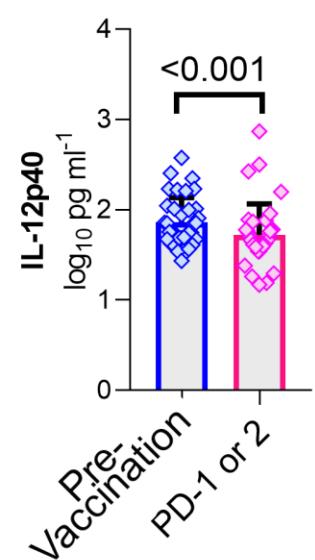
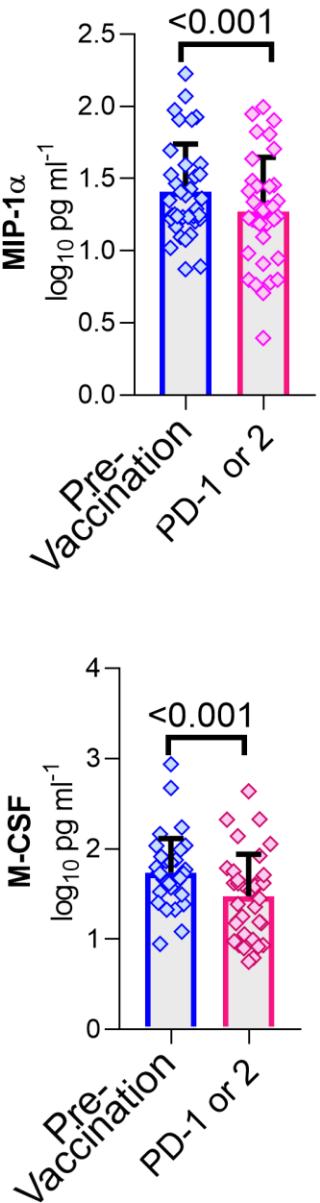
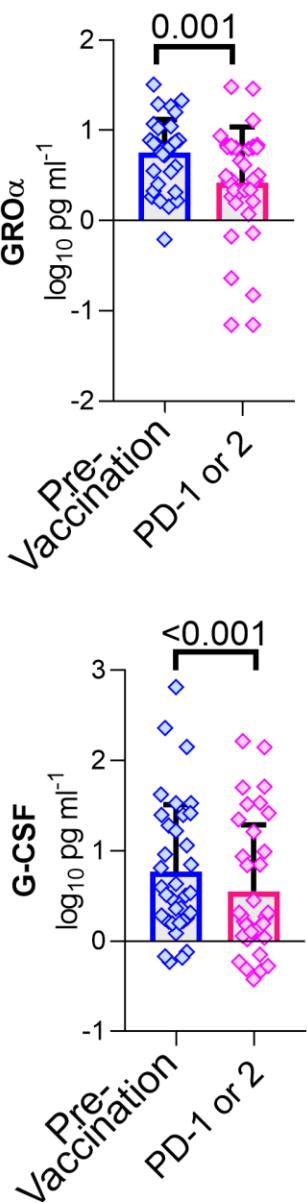
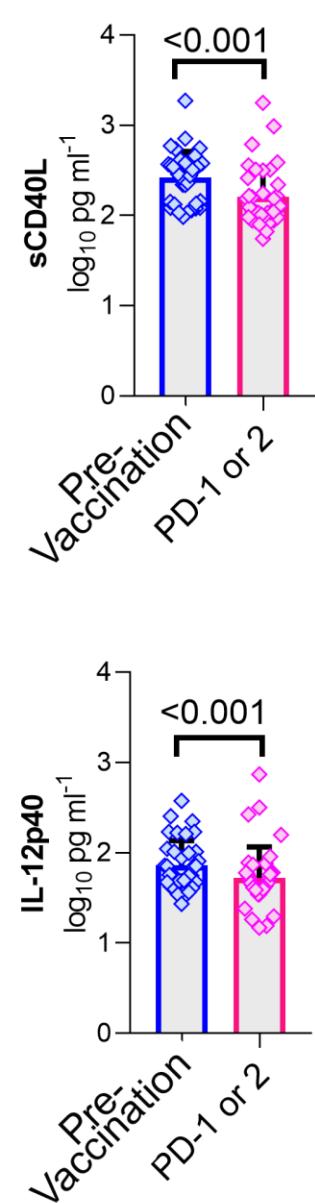
Post-dose 1

Post-dose 2

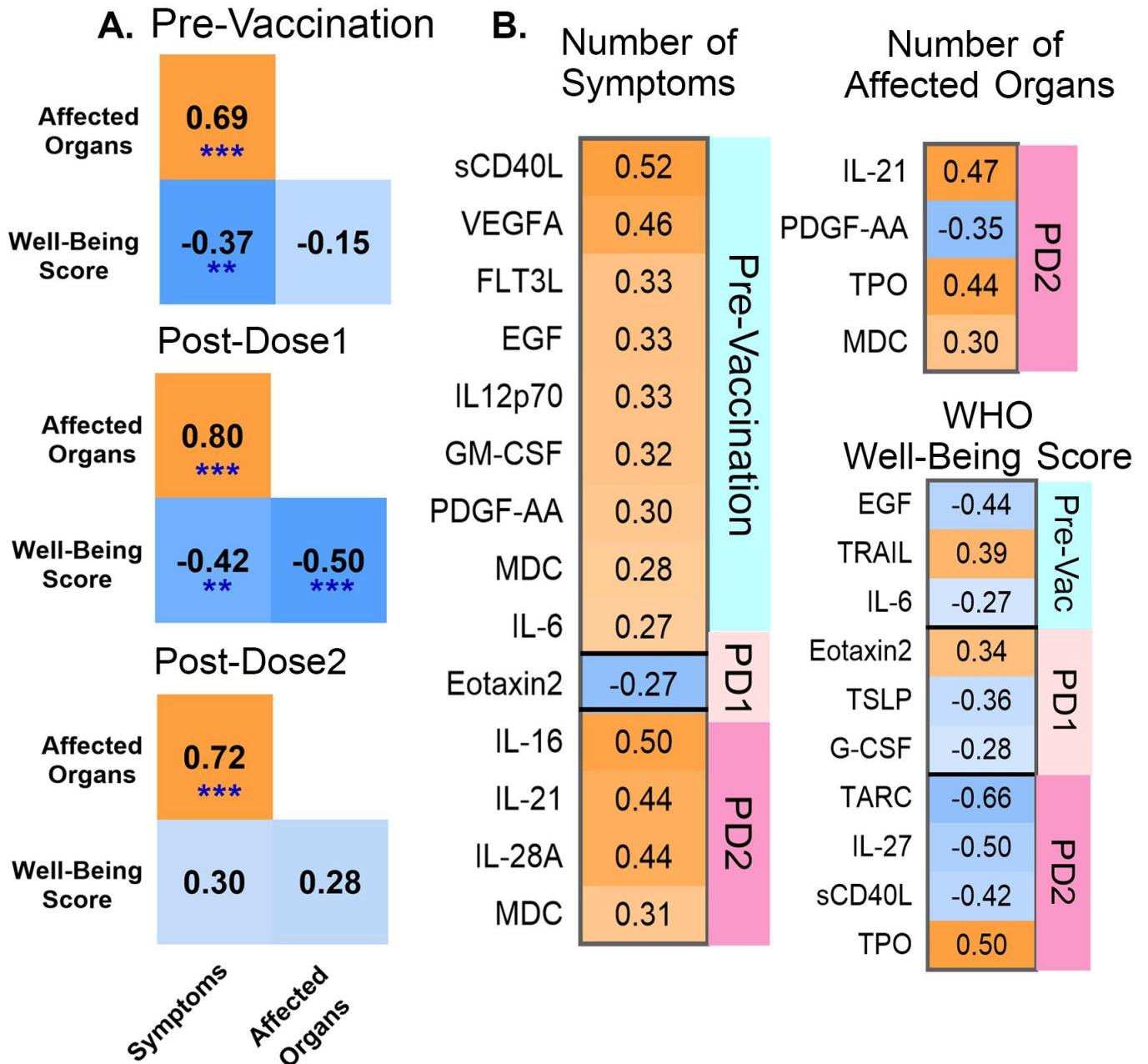
Impact of vaccination on markers of systemic inflammation



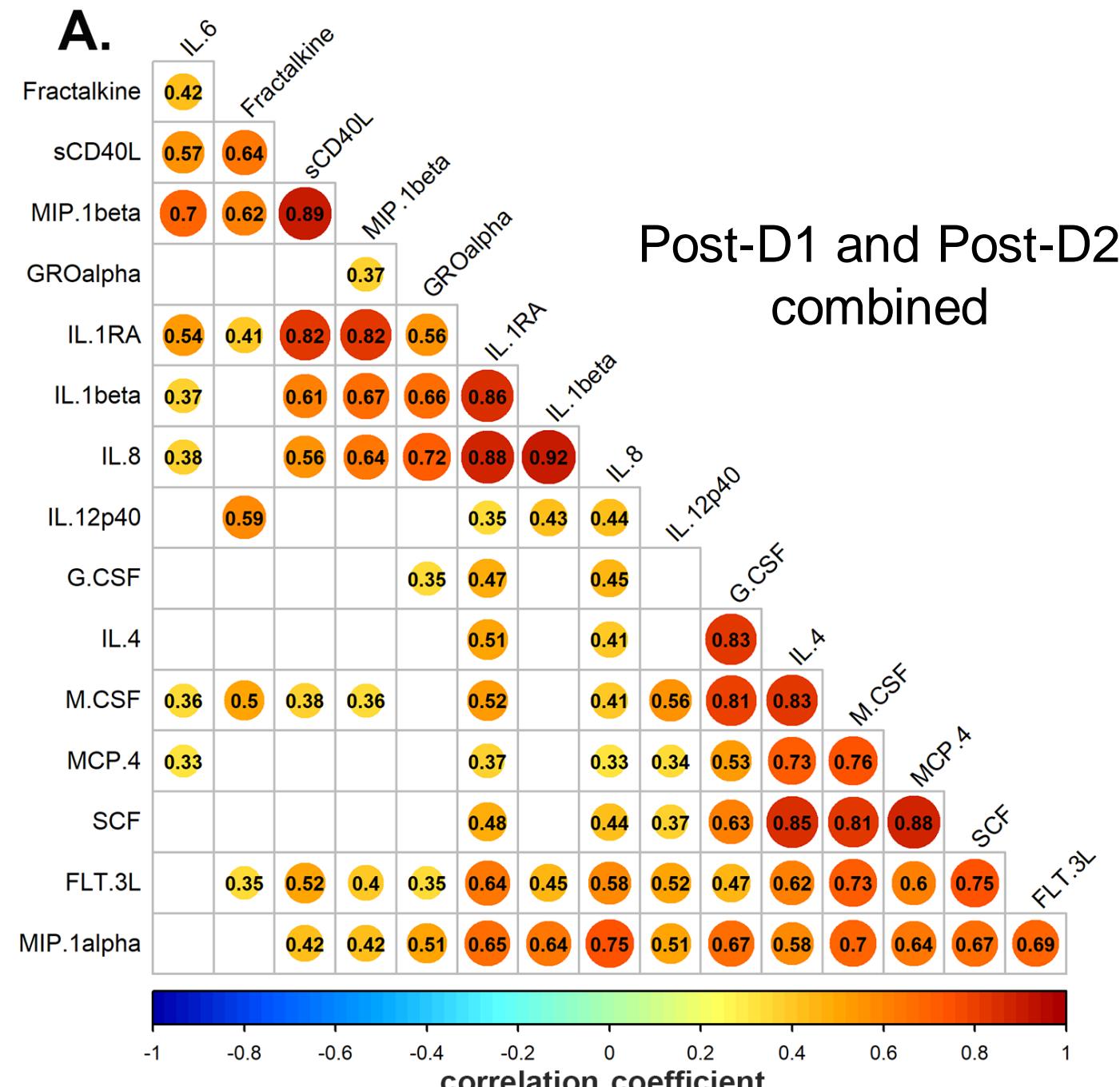
Post-dose 1 or 2



Correlations between plasma cytokine/chemokine levels and clinical parameters

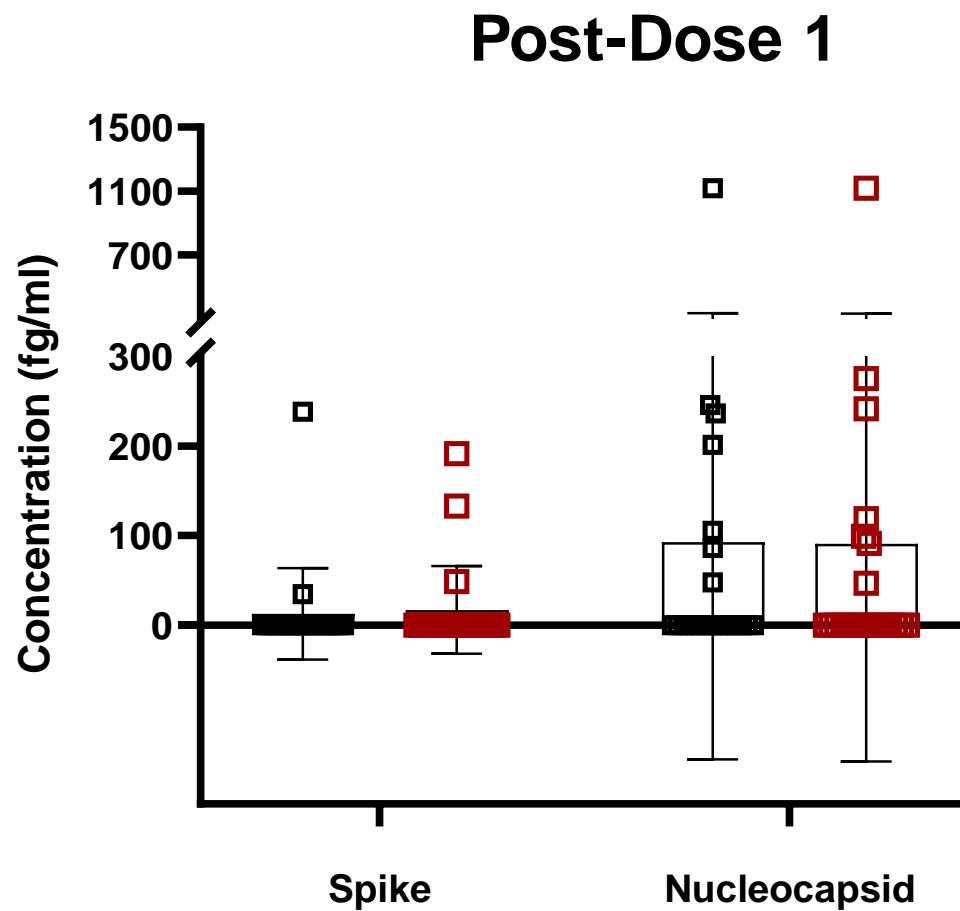


Correlations between plasma cytokine/chemokine levels

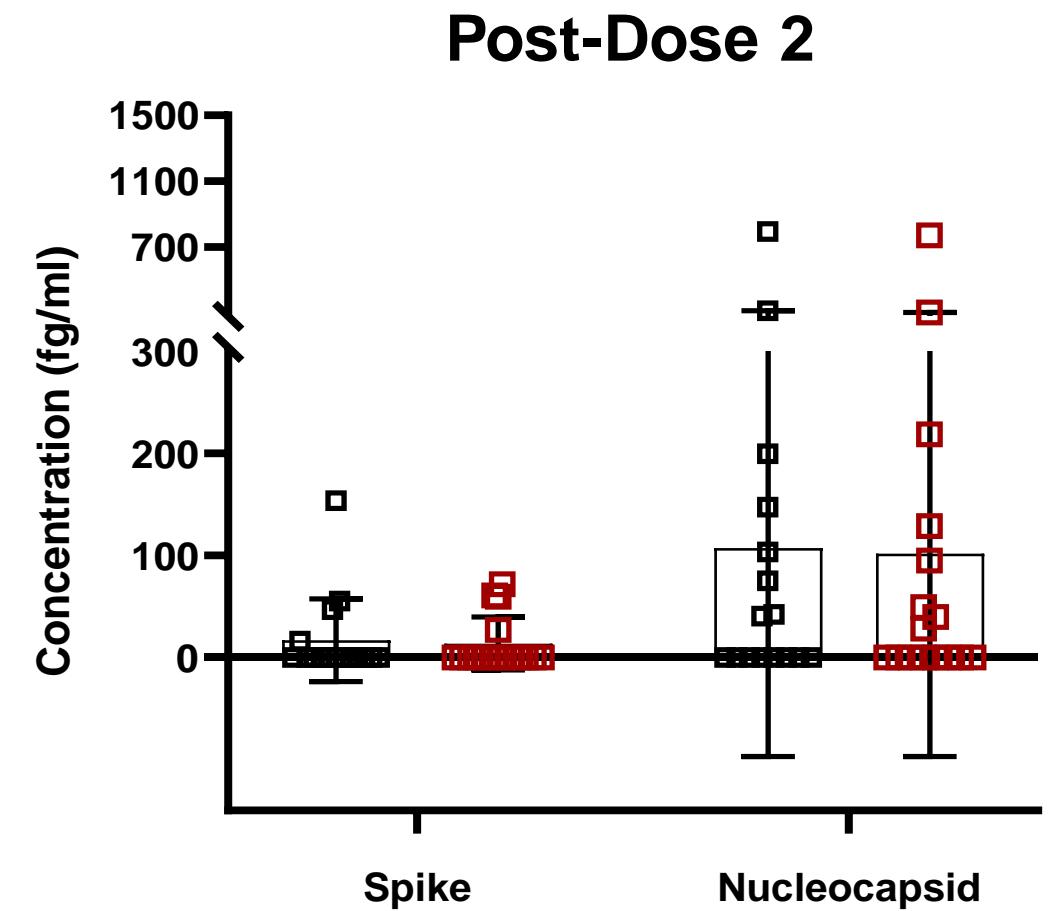


Soluble spike and nucleocapsid protein levels in the plasma of patients with PCC

◻ Pre-vaccination ◻ Post-vaccination_1 dose

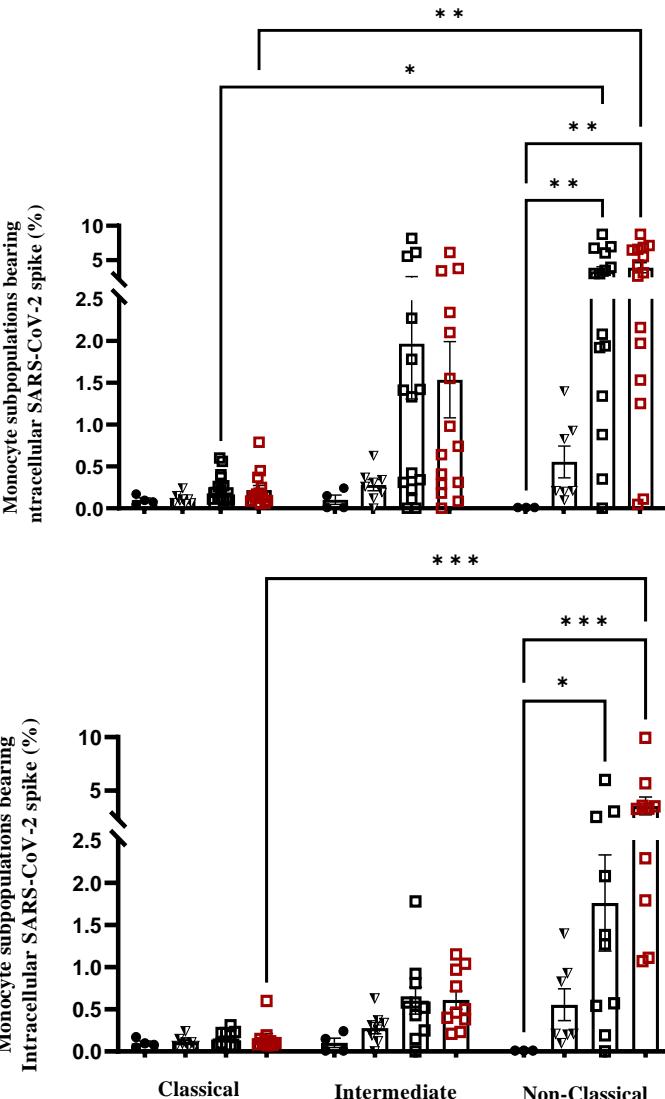
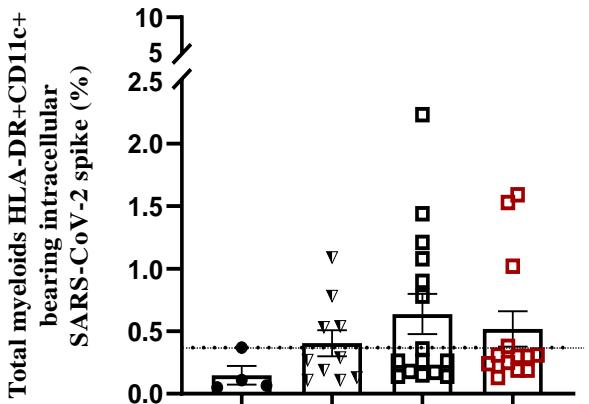


◻ Pre-vaccination ◻ Post-vaccination_2 doses



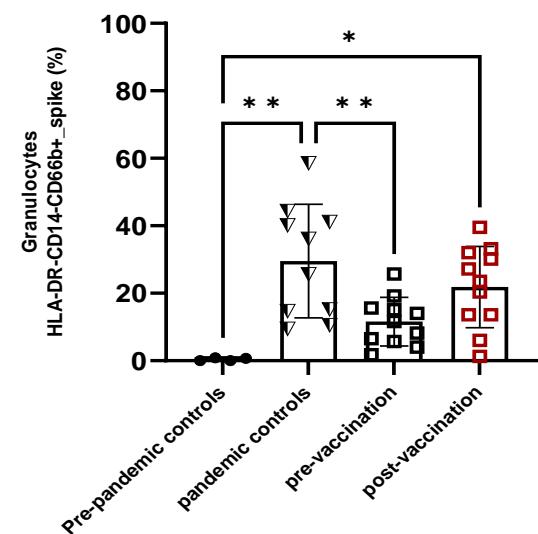
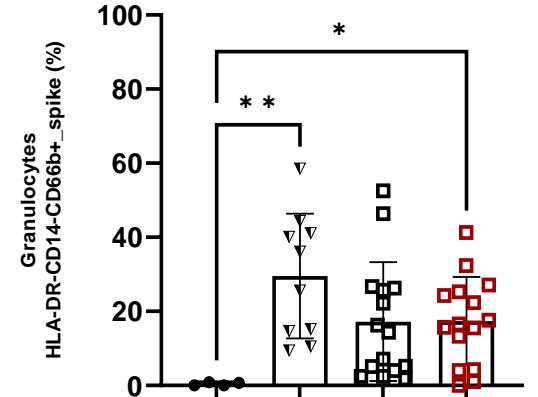
Intracellular SARS-CoV-2 Spike S1 protein in monocyte subpopulations and granulocytes

Post-Dose 1



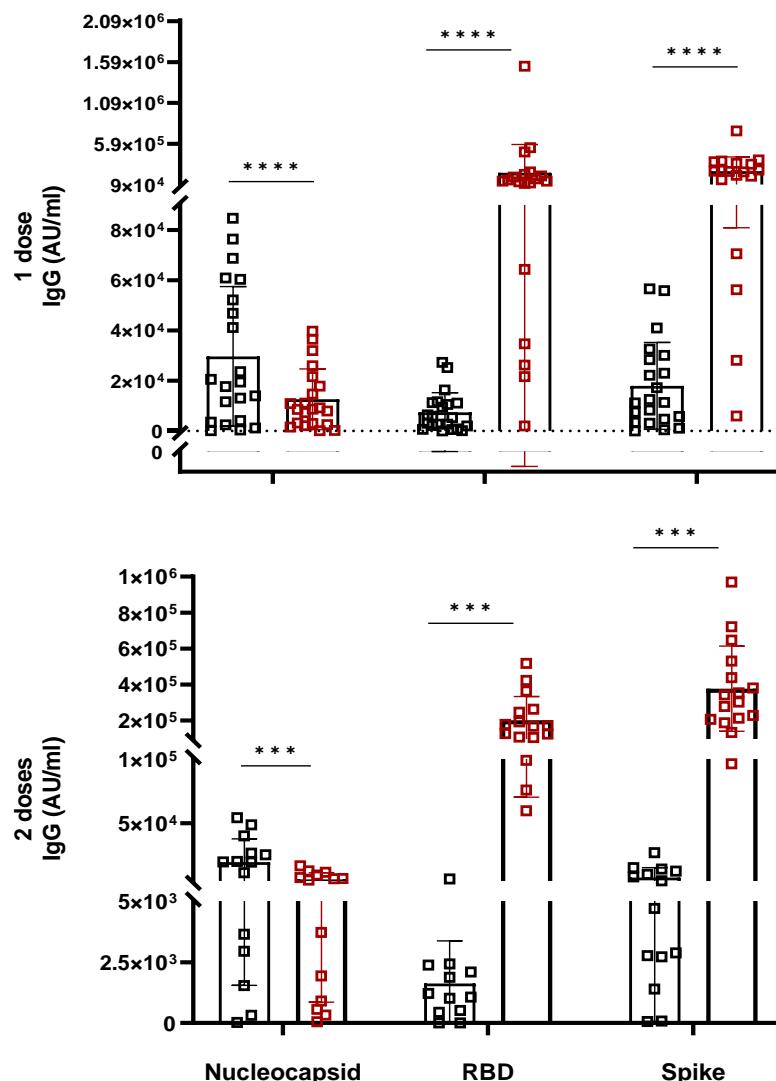
Legend:

- pre-pandemic controls
- pre-vaccination
- ▽ pandemic controls
- post-vaccination

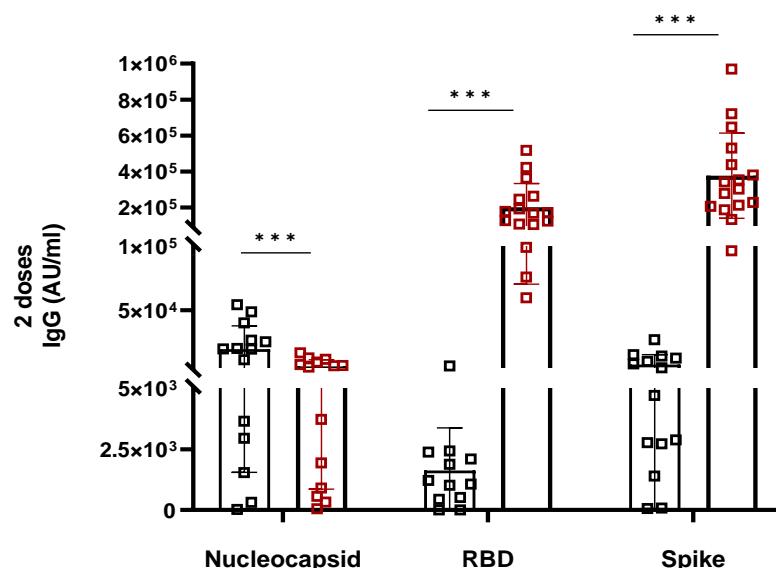


Plasma levels of IgG and IgM recognizing SARS-CoV-2 nucleocapsid, RBD and spike antigens

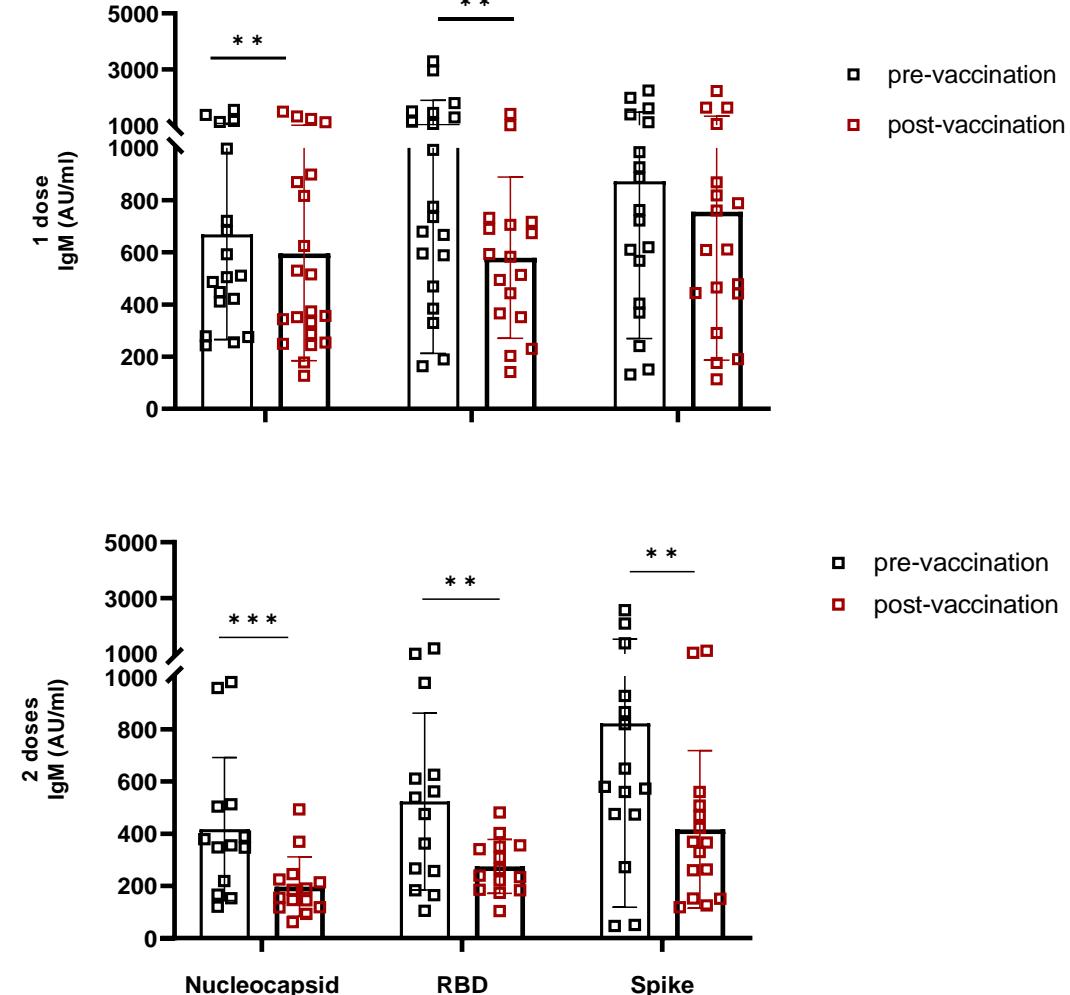
1 vaccine dose



2 vaccine doses



IgG levels



IgM levels

Conclusions and Lessons Learned

- COVID-19 vaccination may decrease PCC symptoms by decreasing certain aspects of systemic inflammation and regulating immune responses but not by clearing persistent viral antigens.
- COVID-19 may result in the establishment of a viral reservoir that requires additional mechanisms for clearance.

Acknowledgments – Co-Authors

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et Innovation**



A special thanks to all our valued patients and our patient-partners!

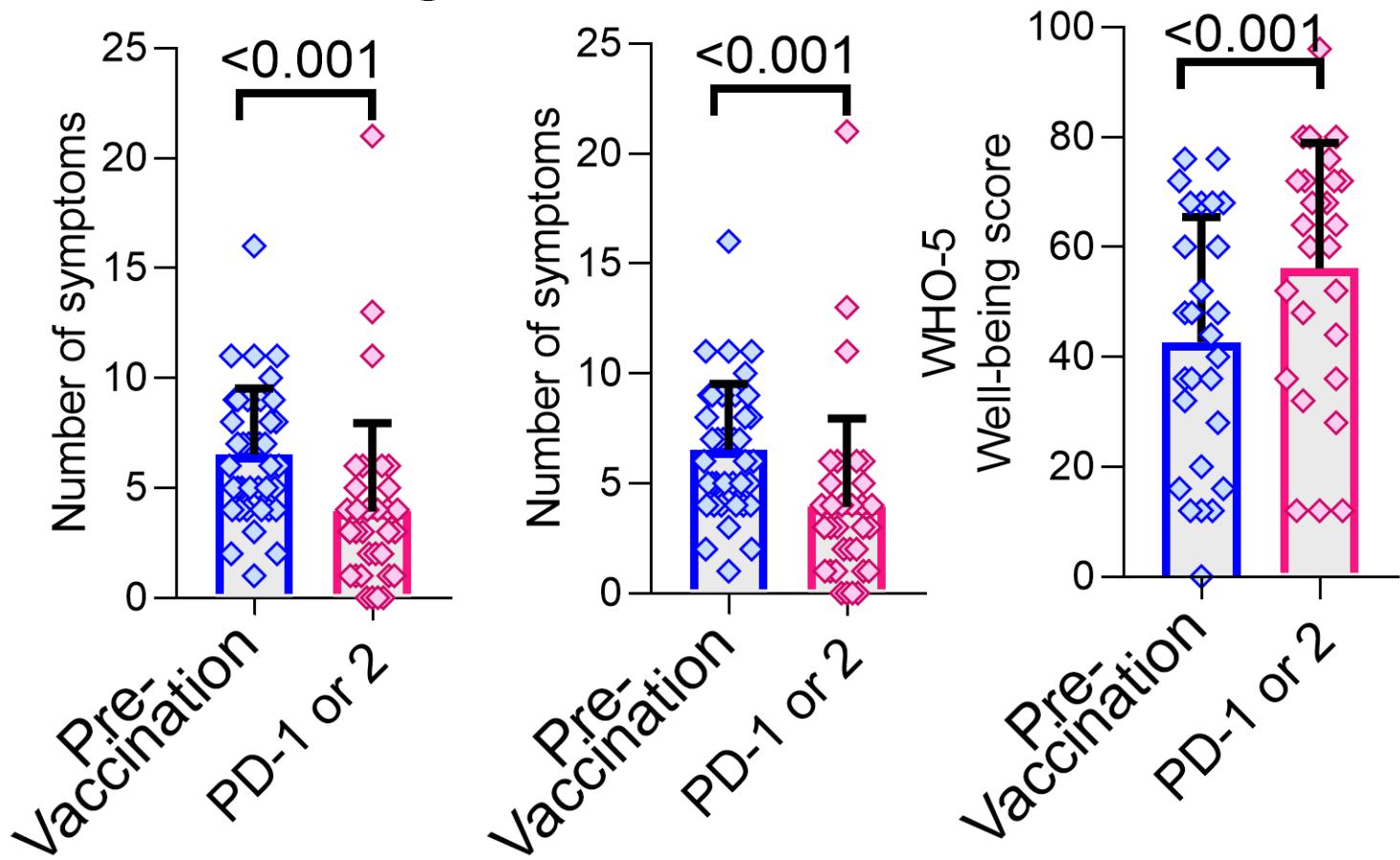
Impact of vaccination on PCC symptoms and clinical tests (PD 1)

	Pre-vaccination	Post-dose 1	P value
CBC ¹			
Hg below normal range, n (%)	0 (0)	2 (9.1)	NA
Total WBC ($10^9/L$; mean (SD))	5.07 (1.05)	5.20 (1.05)	0.71
Lymphocyte count ($10^9/L$; mean (SD))	1.58 (0.43)	1.64 (0.49)	0.21
Platelets ($10^9/L$; mean (SD))	260.59 (43.18)	259.09 (47.63)	0.83
MPV (fL; mean (SD))	8.86 (0.70)	8.77 (0.70)	0.29
Markers of inflammation			
CRP (>10.0 mg/L; n (%)) ²	0 (0)	0 (0)	NA
D-Dimer ($\mu g/L$; >600; n (%)) ³	1 (6.7)	1 (6.7)	1
Ferritin ($\mu g/L$; mean (SD)) ⁴	71.70 (62.08)	62.10 (46.99)	0.03
Fibrinogen (g/L; mean (SD)) ⁵	3.53 (0.64)	3.34 (0.68)	0.19
≥ 1 ongoing PCC symptom, n (%)	23 (100)	20 (87)	NA
Number of PCC symptoms, mean (SD)	6.57 (3.49)	4.65 (4.95)	0.005
Number of affected organ systems, mean (SD)	3.09 (1.00)	1.91 (1.24)	<0.001
WHO-5 Well-Being Index ⁶			
Mean (SD)	48.44 (19.45)	61.11 (17.45)	0.001
Score ≤ 50 , n (%)	9 (50)	5 (27.8)	0.22

Impact of vaccination on PCC symptoms and clinical tests (PD 2)

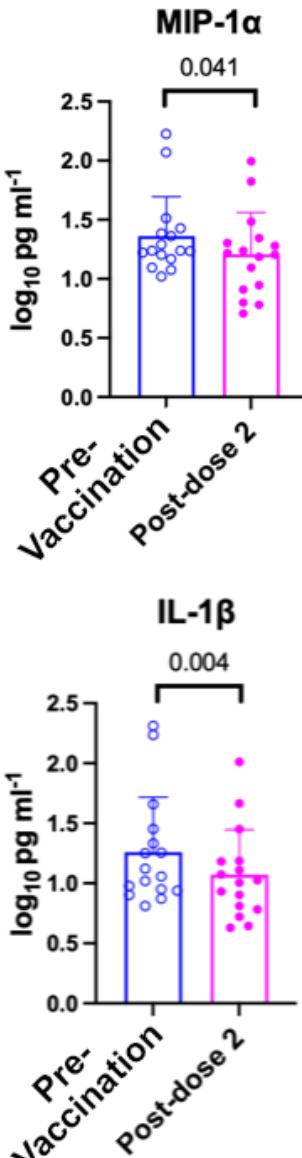
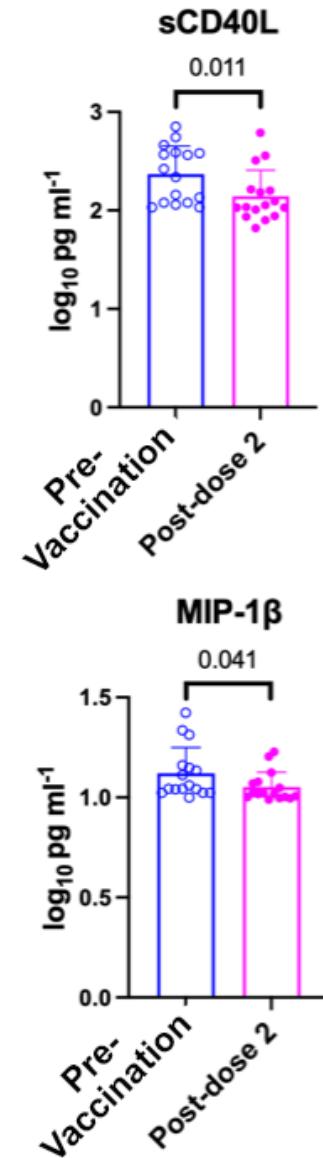
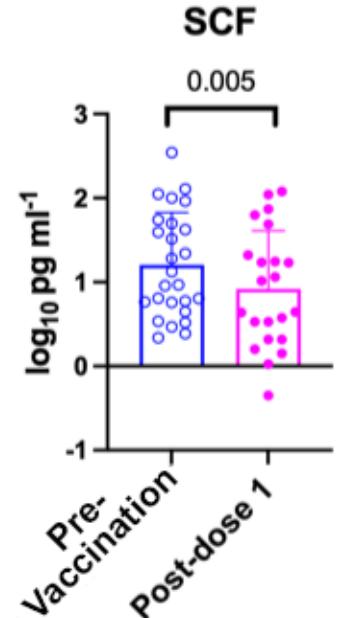
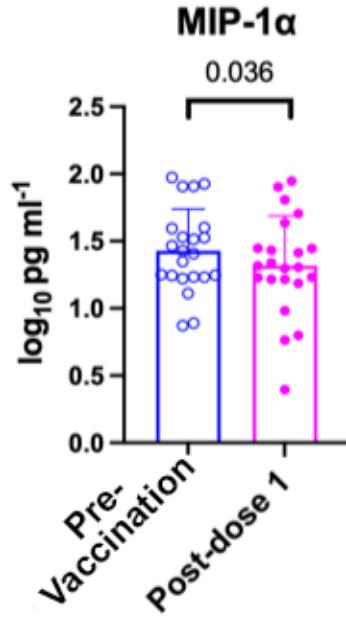
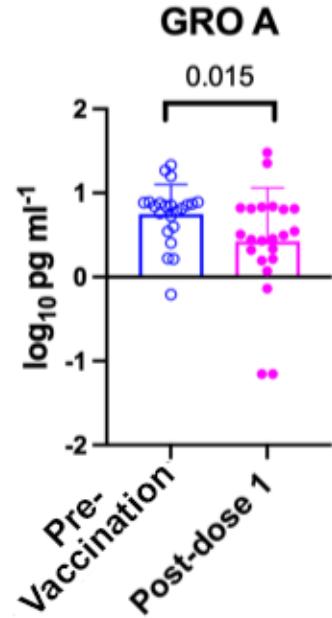
	Pre-vaccination, n=16	Post-dose 2, n=16	P value
CBC ¹			
Hg below normal range, n (%)	5 (38.5)	4 (30.8)	1
Total WBC (10 ⁹ /L; mean (SD))	5.35 (1.27)	5.35 (1.20)	1.00
Lymphocyte count	1.62 (0.40)	1.71 (0.46)	0.59
Platelets (10 ⁹ /L; mean (SD))	248.92 (45.68)	250.85 (66.39)	0.86
MPV (fL; mean (SD))	8.66 (0.80)	8.50 (0.99)	0.22
Markers of inflammation			
CRP (>10.0 mg/L; n (%)) ²	0 (0)	0 (0)	NA
D-Dimer (μ g/L; >600; n (%)) ³	1 (8.3)	3 (25)	0.5
Ferritin (μ g/L; mean (SD)) ⁴	92.75 (55.88)	79.42 (51.49)	0.04
Fibrinogen (g/L; mean (SD)) ⁵	3.71 (0.66)	3.67 (0.99)	0.79
≥ 1 ongoing PCC symptom, n (%)	16 (100)	14 (87.4)	NA
Number of PCC symptoms, mean (SD)	6.44 (2.37)	3.38 (2.60)	<0.001
Number of affected organ systems, mean (SD)	3.25 (1.07)	1.88 (1.09)	<0.001
WHO-5 Well-Being Index ⁶			
Mean (SD)	34.55 (24.15)	47.64 (27.10)	0.09
Score ≤ 50 , n (%)	9 (81.8)	5 (45.5)	0.12

Impact of vaccination on PCC Symptoms

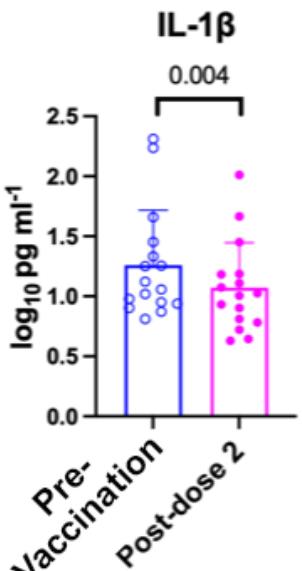
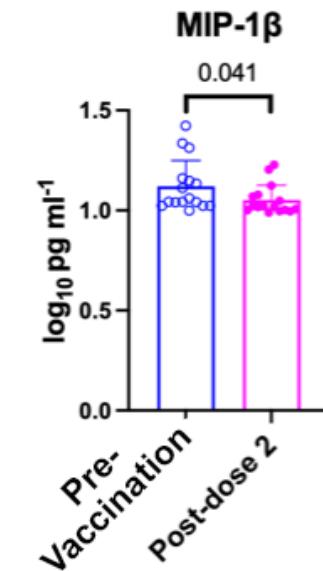


Post-dose 1 or 2

Impact of vaccination on markers of systemic inflammation

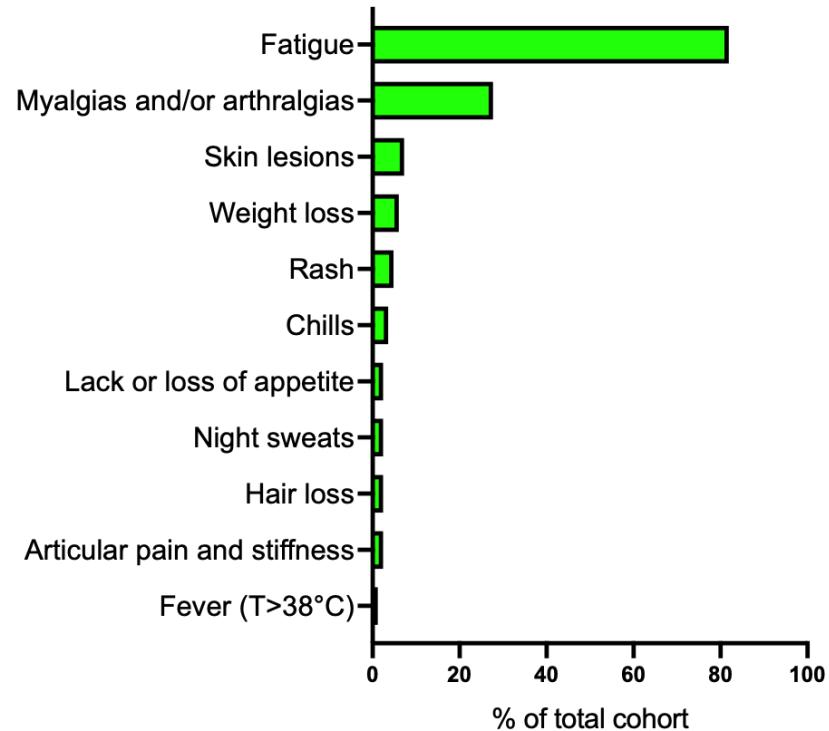


Post-dose 1

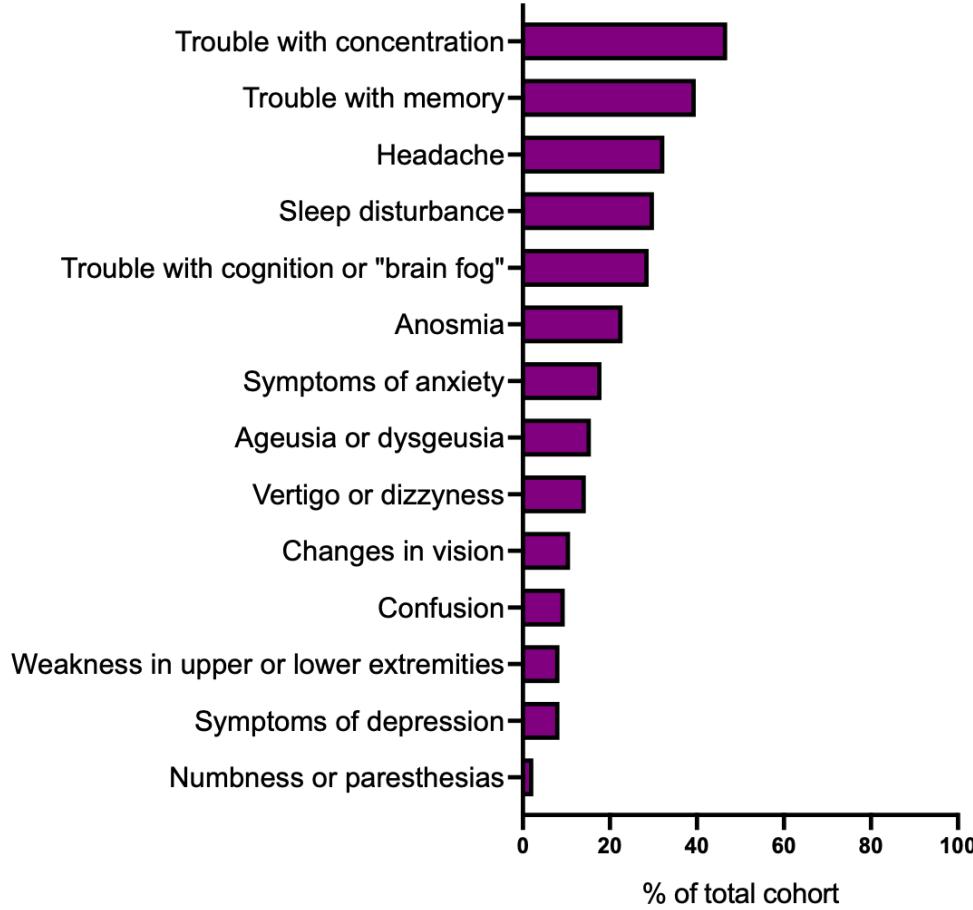


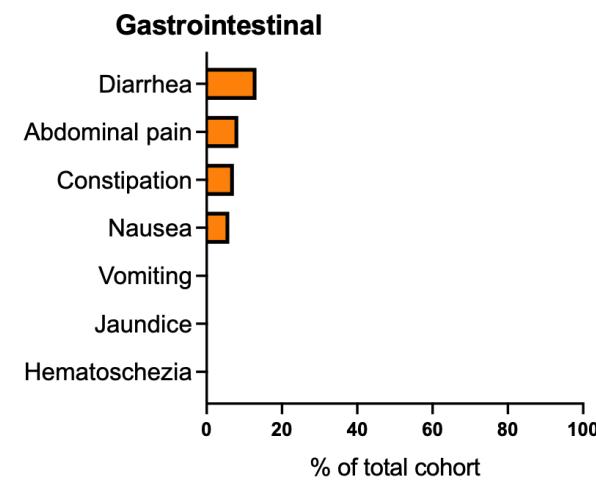
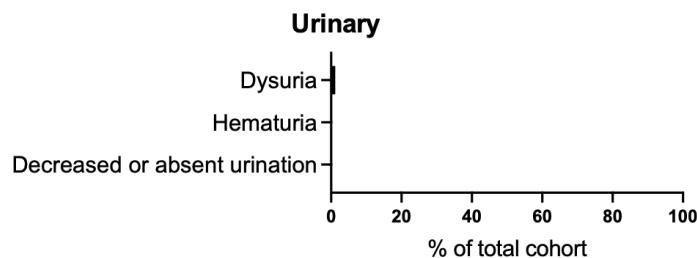
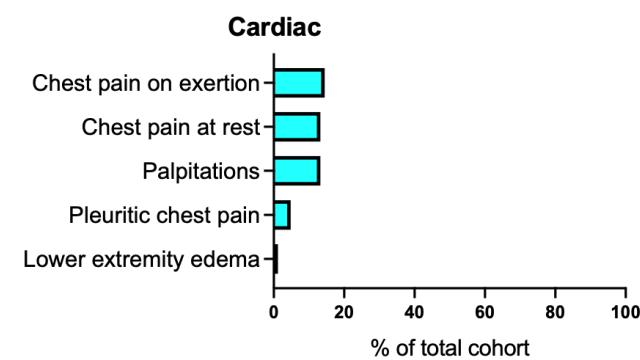
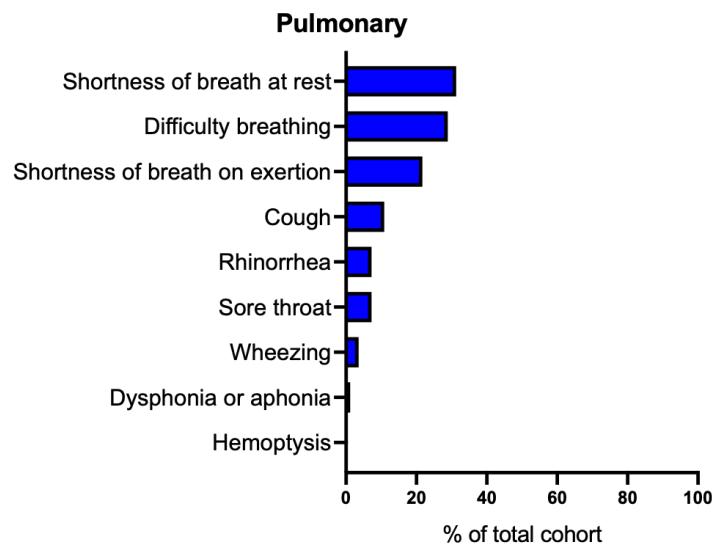
Post-dose 2

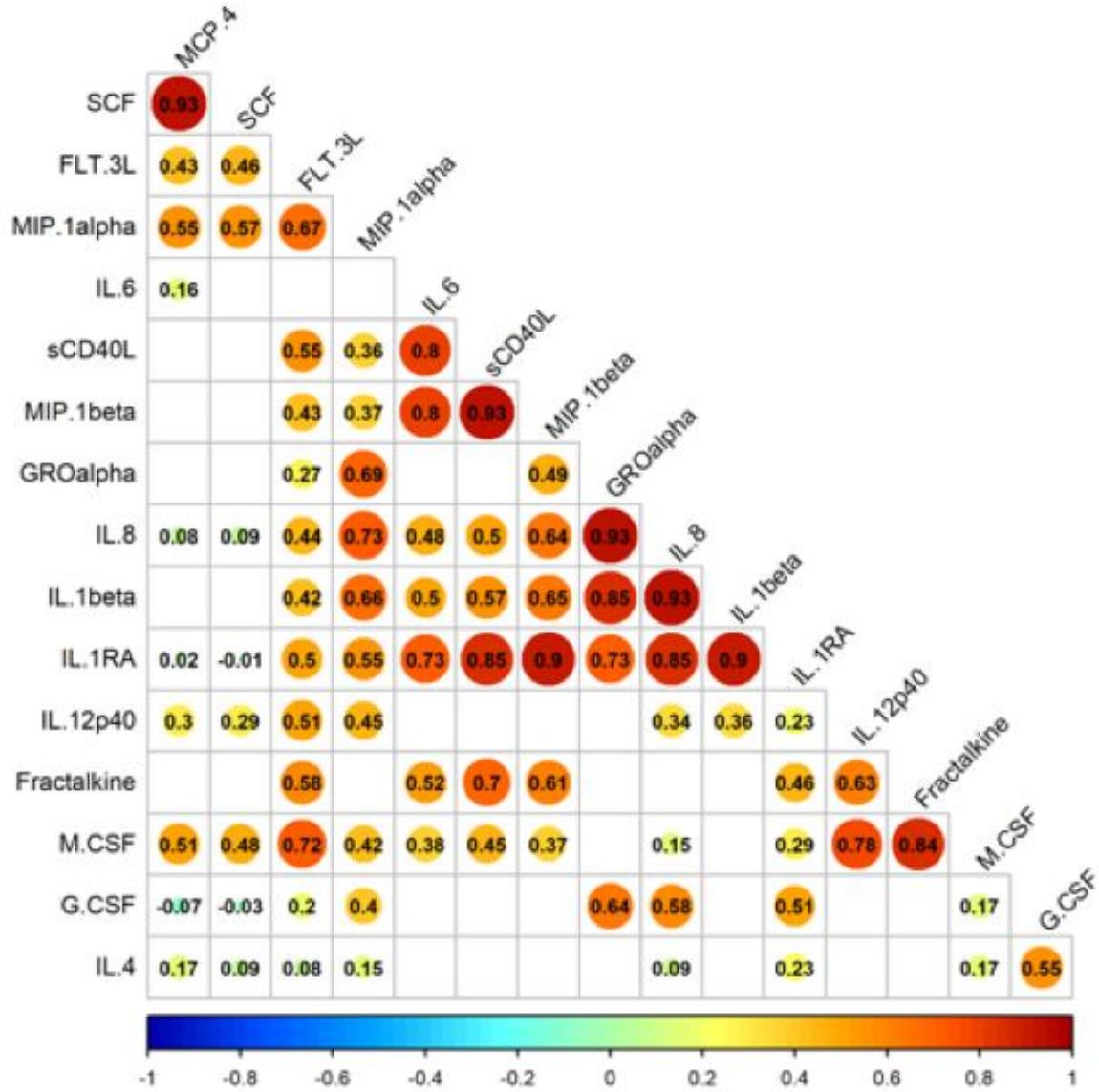
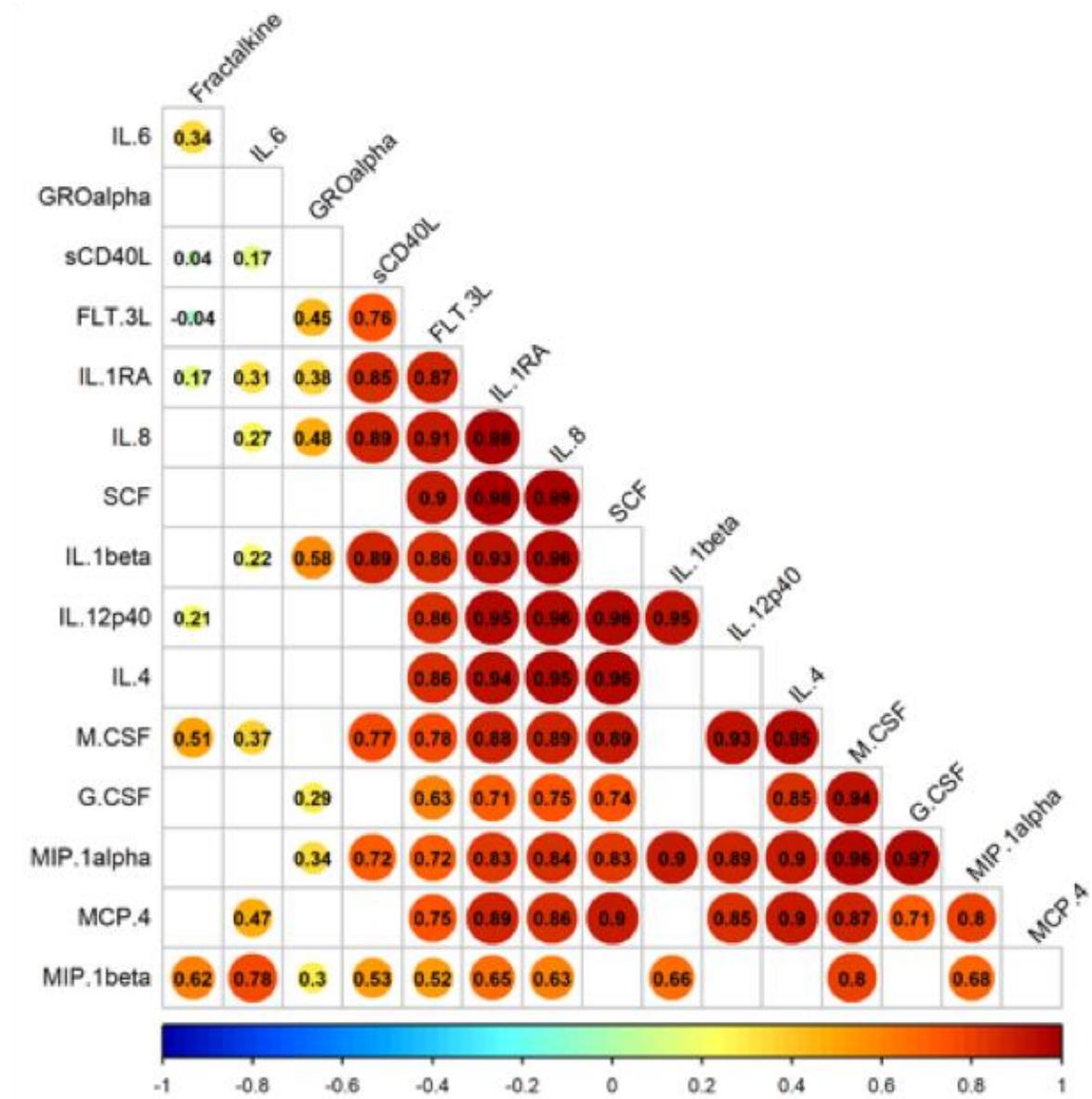
Systemic, musculoskeletal and dermatological

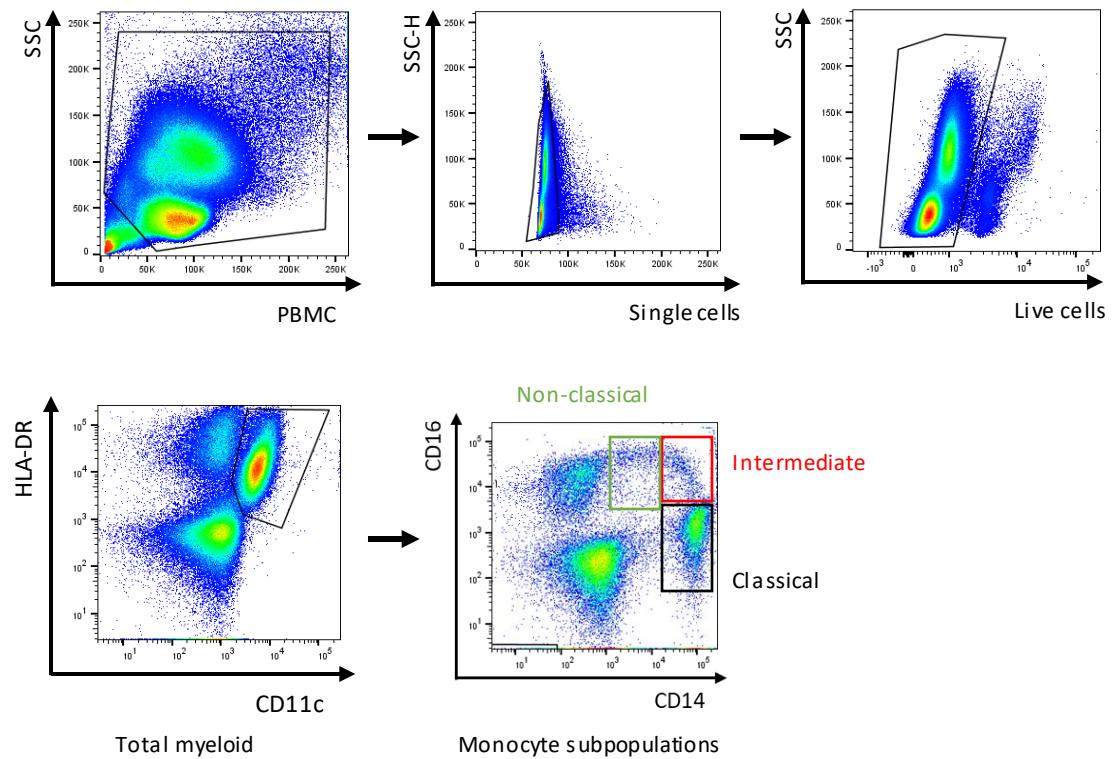


Neuropsychological





A. Post-dose 1**B. Post-dose 2**

A-**B-**