RISK FACTORS FOR NEW-ONSET AUTOIMMUNE DISEASES IN LONG COVID PATIENTS: A REAL-WORLD COHORT

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Long Covid complexity

What do we know?

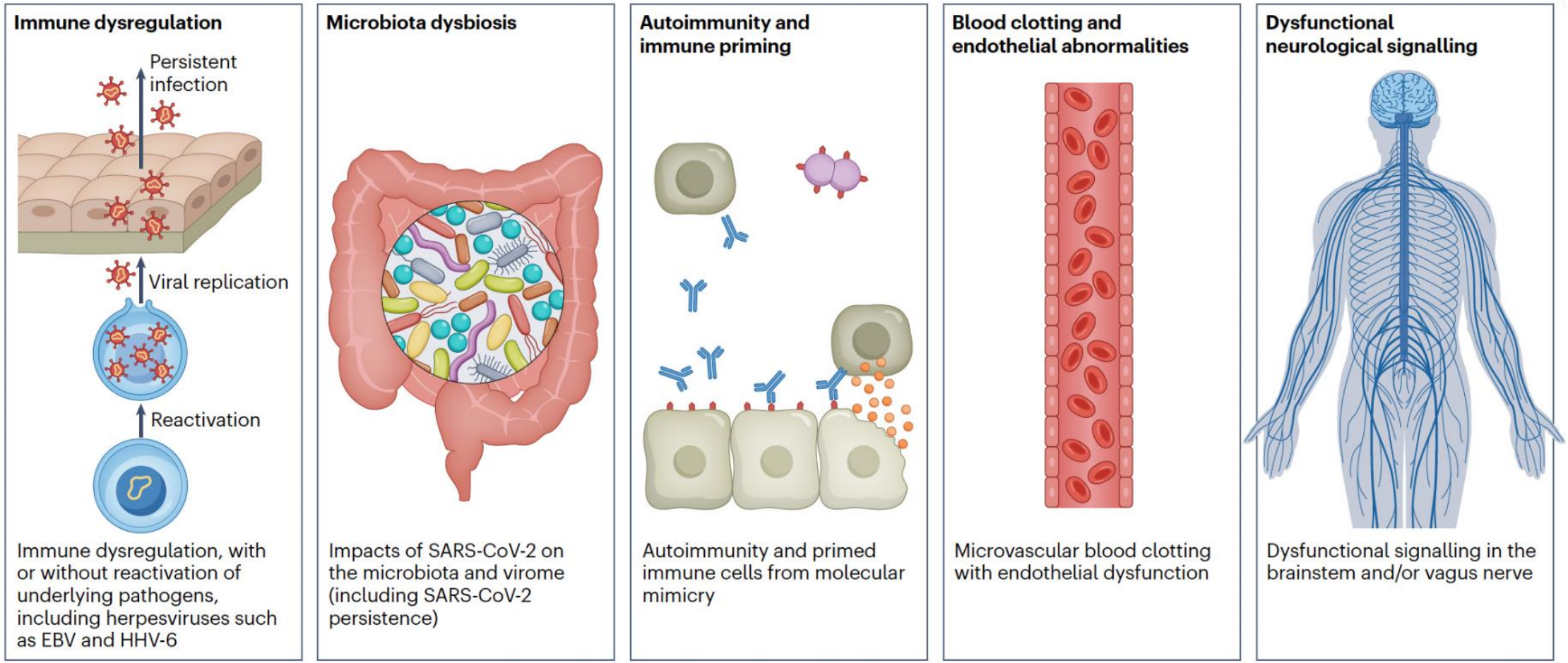


Fig. 3 | Hypothesized mechanisms of long COVID pathogenesis.

Hannah E. Davis, Lisa McCorkell, Julia Moore Vogel & Eric J. Topol
Nature Reviews Microbiology volume 21, pages133–146 (2023)

Patients & Methods

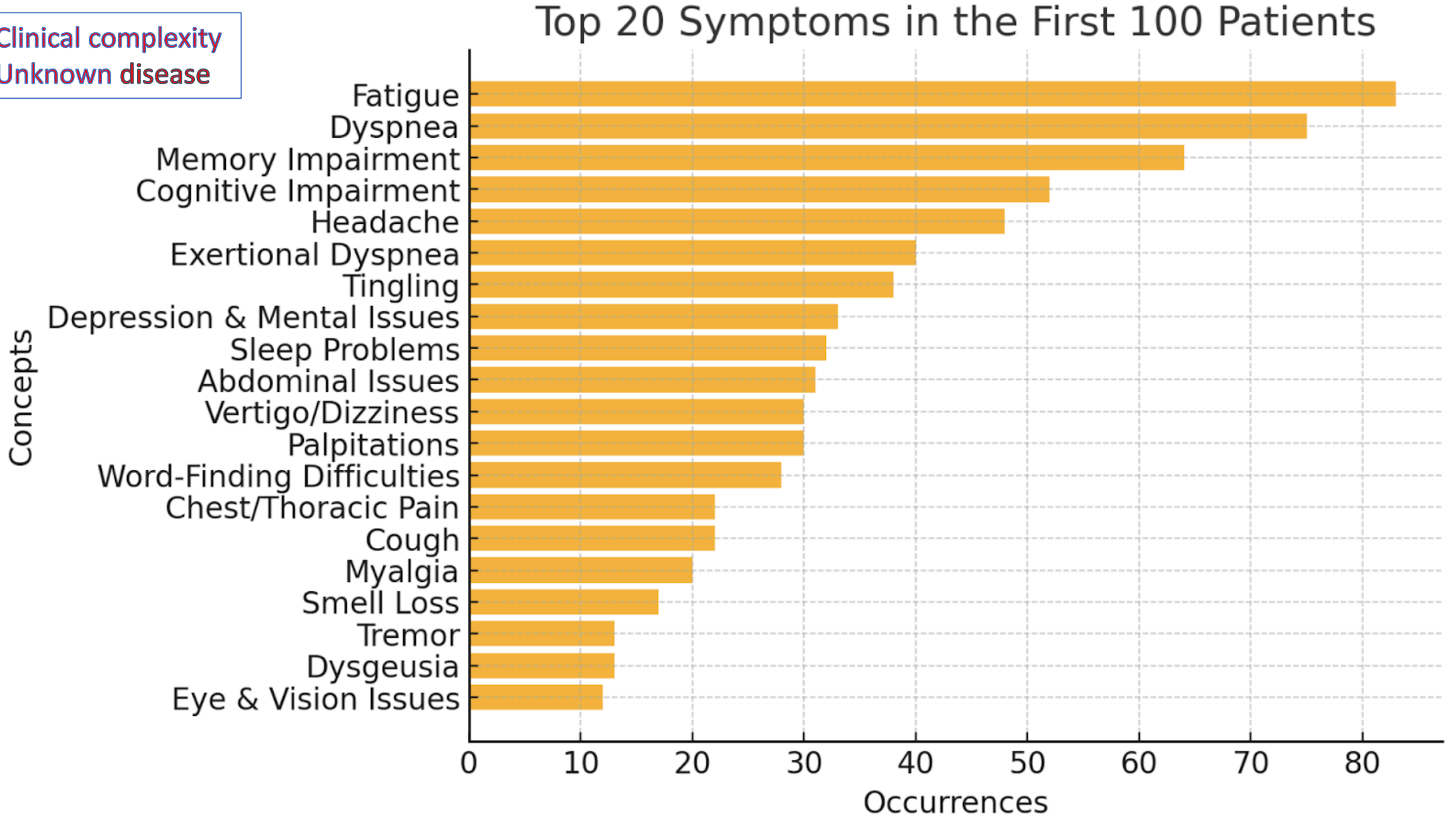
1. **Real-world cohort:** family practice-based >250 patients, ongoing since July 2021
   → Fully detailed electronic health records (ICPC & HPO)

2. Use of validated clinical scales for both clinicians (Severity-DUSOI) & patients (PROMs-Patient Reported Outcome Measures; COOP chart)

3. Uniform treatment scheme for all patients
   →anticoagulants;1st line, antivirals 2nd line

4. Long-term follow-up (average > 2 years, total 220 person-years)

Clinical complexity
Unknown disease



Man, 65, retired accountant Case MGA.065

T89 - Type 1 Diabetes (IDDM) – 1998

T82 - Obesity with BMI ≥ 30 - August 2010

A89 - Colostomy for cancer - 2011

K75 - Dilated cardiac infarction - 2015

A77 - COVID-19 - September 2022

D84 - Post-COVID gastroparesis - December 2022

B83 - Post-COVID blood coagulation disorder - January 2023

B83 - Post-COVID antiphospholipid syndrome - August 2023

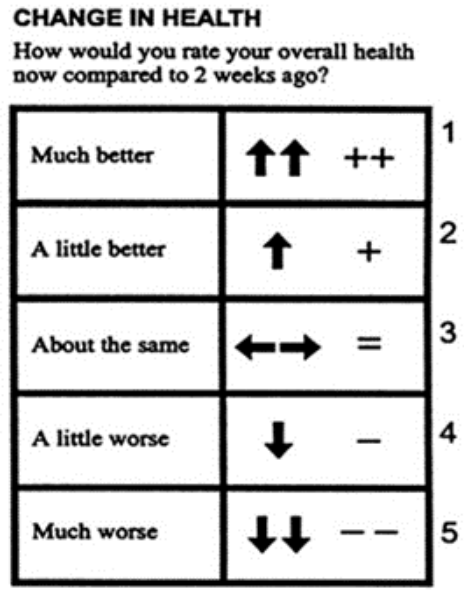
K90 - Post-COVID stroke - October 2024

N19 - Post-COVID aphasia - December 2024

ICPC-2 coded multimorbidity

DUSOI severity: 3 out of 4 (clinician-reported)

COOP Functional status: 27 out of 30 (patient-reported)



HPO coded symptoms 2023

Ground-glass opacities (HP:0033564) [multiple diffuse micro-opacities of both lung fields]; **Fatigue** (HP:0012378) [general tiredness]; **Distractibility** (HP:0000736); **Gait disturbance** (HP:0001288) [misses steps on stairs]; **Immediate memory impairment** (HP:0031346) [small decrease]; **Word-finding difficulty** (HP:0031003) [loss of word]; **Forgetfulness** (HP:0002364) [misses some names]; **Chronic cough** (HP:0012735) [some cough].

Blood viral RNA at 2 years : 1611 counts

Jamoulle et al. *Viruses* 2022

Risk factors incident autoimmune disease:

multivariable logistic regression (on 111 patients)

Variable	Odds Ratio	95% CI	P value
Age	0.97	0.92 - 1.02	0.20
Sex (F)	4.42	1.12-22.13	0.047
COOP-change	2.42	1.15-5.81	0.044
Vaccination	0.092	0.0078-0.60	0.018

Corrected for comorbidities, #acute COVID episodes and COVID wave/variant

- Age does not influence autoimmunity
- Women > 4-fold higher odds
- PROMS: higher COOP-change score at baseline >2-fold higher odds
- Vaccination lowers odds of having incident autoimmune disease by >90%
- Multivariable model significantly predicted new-onset autoimmune disease (AUROC 0.79 [0.67-0.92], p=0.0002).

Jamoulle et al. unpublished

Blood transcriptomic analyses reveal persistent SARS-CoV-2 RNA & immunometabolism associated with Long Covid

KU LEUVEN

Soraya Maria Menezes

Johan van Weyenbergh

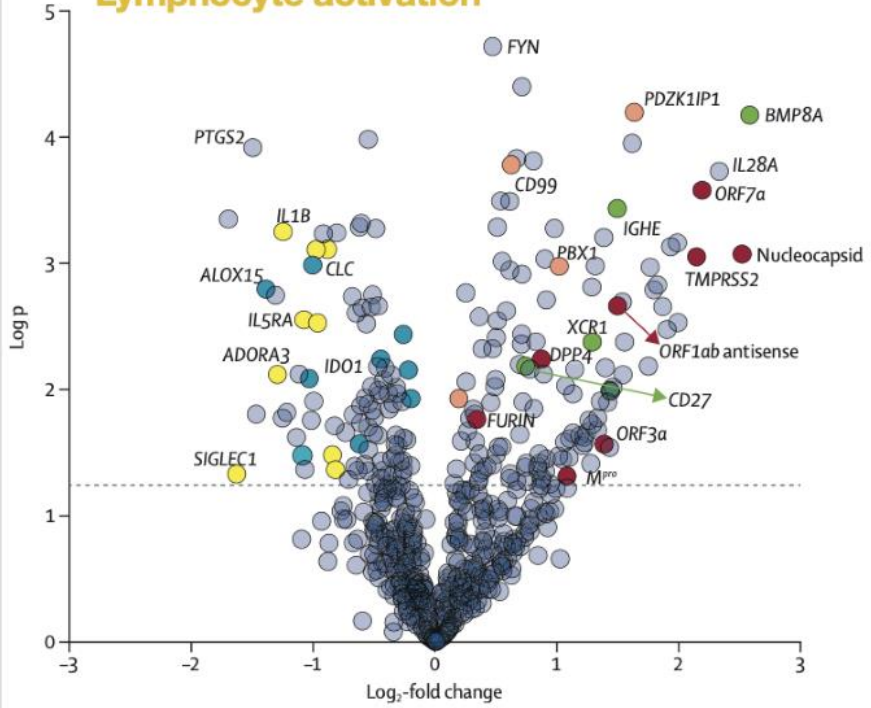
Viral RNA and SARS-COV-2-associated host

Memory B-cell

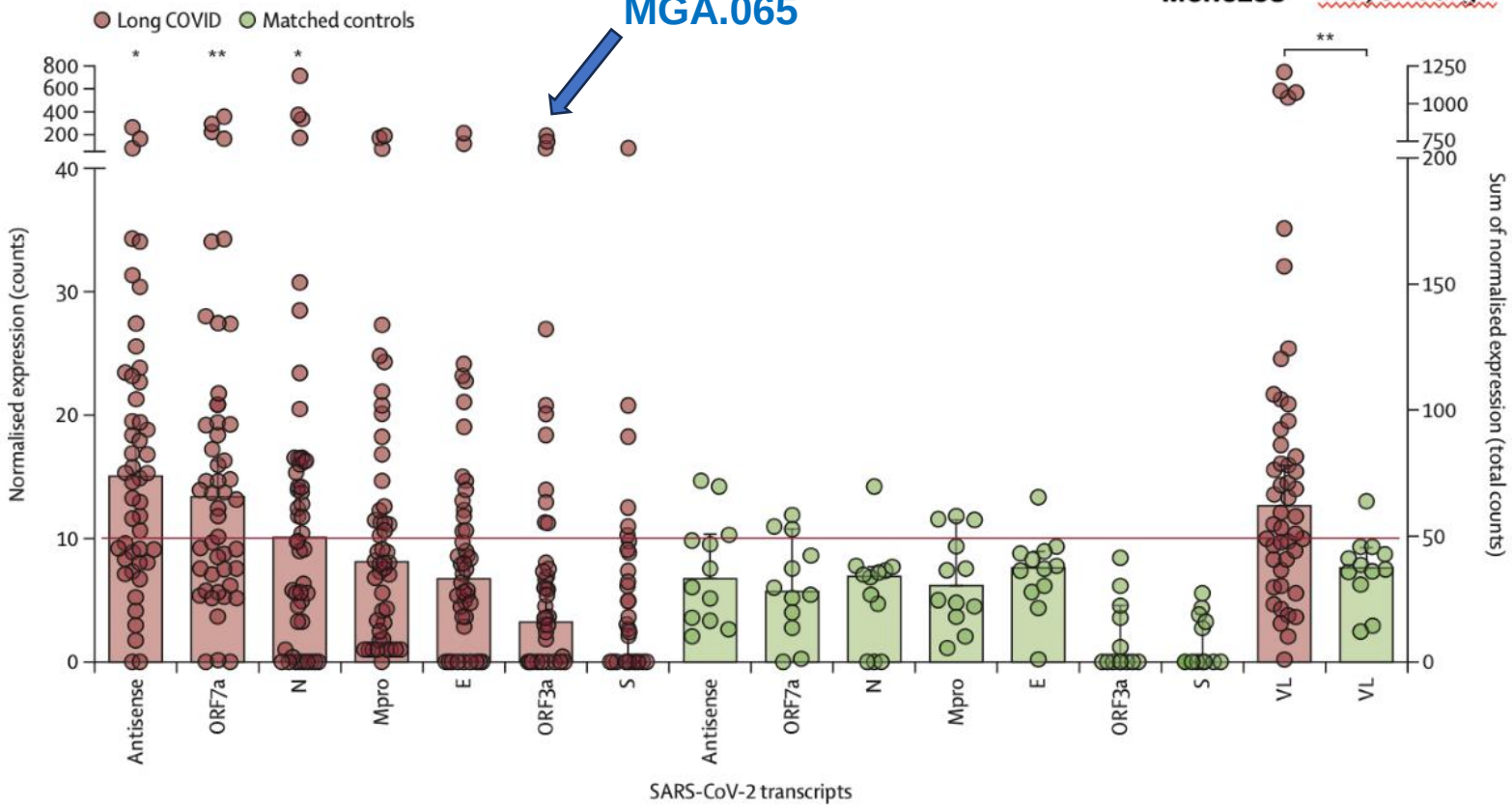
Platelet-expressed

Immunometabolism

Lymphocyte activation

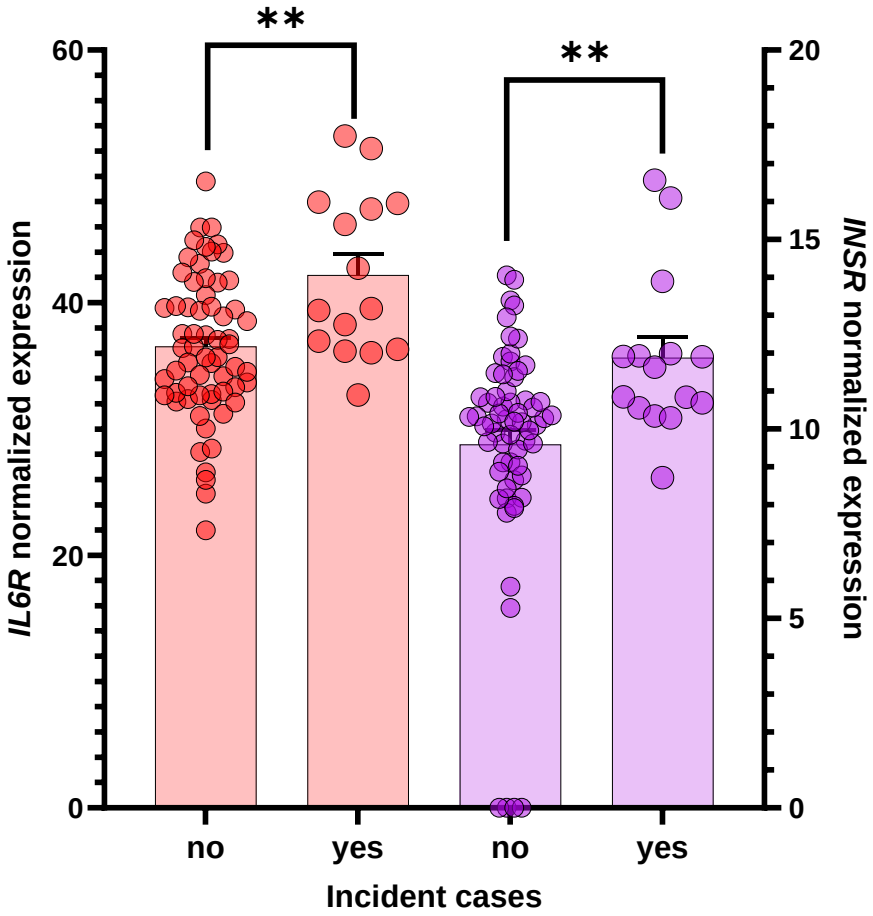


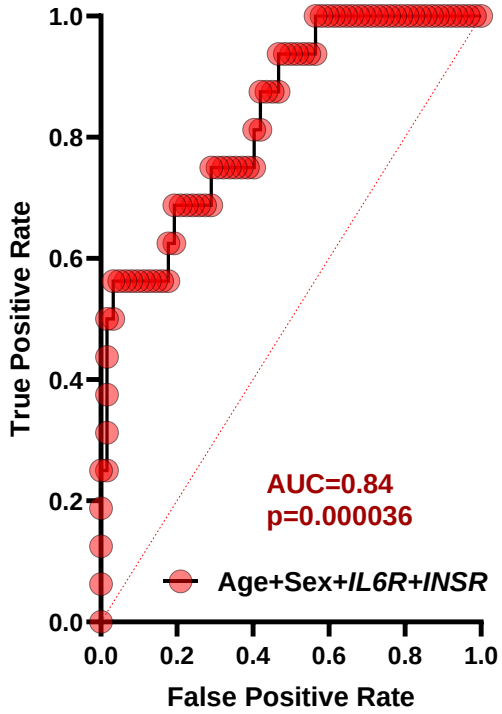
MGA.065



Menezes SM et al. Blood transcriptomic analyses reveal persistent SARS-CoV-2 RNA and candidate biomarkers in post-COVID-19 condition. Lancet Microbe 2024

Results digital transcriptomics:
increase RNA Interleukin-6 receptor & Insulin Receptor post-COVID autoimmunity





Multivariable model significantly predicted new-onset autoimmune disease

Jamoulle et al. unpublished

Conclusions

What a real-world cohort shows us:

1. **In a real-world cohort, female sex and COOP-change score are independent predictors of new-onset autoimmune disease in Long COVID, while SARS-CoV-2 vaccination is protective.**

2. ***IL6R* and *INSR* RNA levels are predictive biomarkers for incident autoimmune disease in Long COVID**

=> early treatment e.g. Tociluzimab, Metformin,…?