GLEM – Clinical Neurology, Saint-Pierre Hospital, Ottignies
7 January 2026

Calendar. ~1500 (Detail)
Leuven, M-Museum

Family Medicine and Unexplained Symptoms

The Case of Long COVID

Marc Jamoulle, MD, PhD
Médecin de famille,
Management Information System HEC ULG
& Centre académique de Médecine Générale (CAMG-UCL)

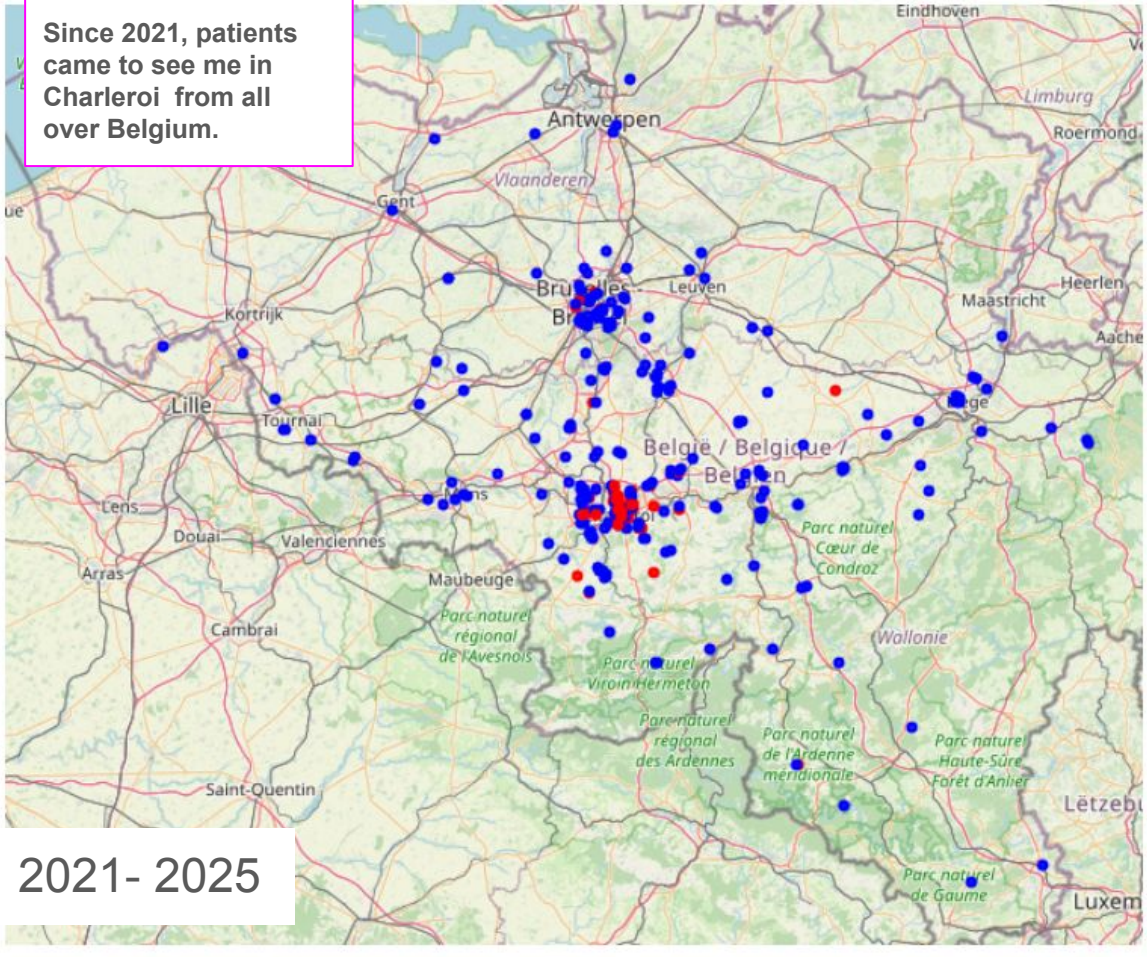
UCLouvain CAMG

LIÈGE université

Conflicts of Interest

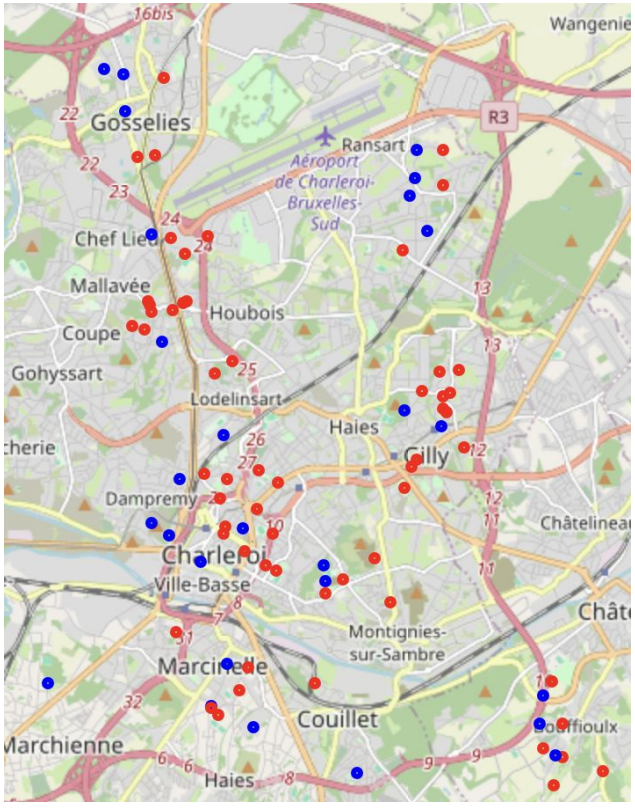
- I earn my living from the care of my patients, which in itself may be considered a conflict of interest.
- In 2022, I received a small, one-time grant from the King Baudouin Foundation, which was not renewed.
- Since 2025, I have been a consultant for the biotechnology company GENCLIS, Nancy, France.

Since 2021, patients came to see me in Charleroi from all over Belgium.



2021- 2025

Figure 2.2 – Distribution of postal codes for patients consulting for suspected Long COVID. Red: 76 patients from the practice's historical panel. Blue: 249 patients with other primary care physicians. Status as of August 29, 2025 (Courtesy of Tarik Jamoulle, data engineer).



Belgium and Charleroi city maps

LC patients
In red: my patients
In blue: those of my colleagues who came to Charleroi for a consultation (2021–2025)

by Dec 21, 2025

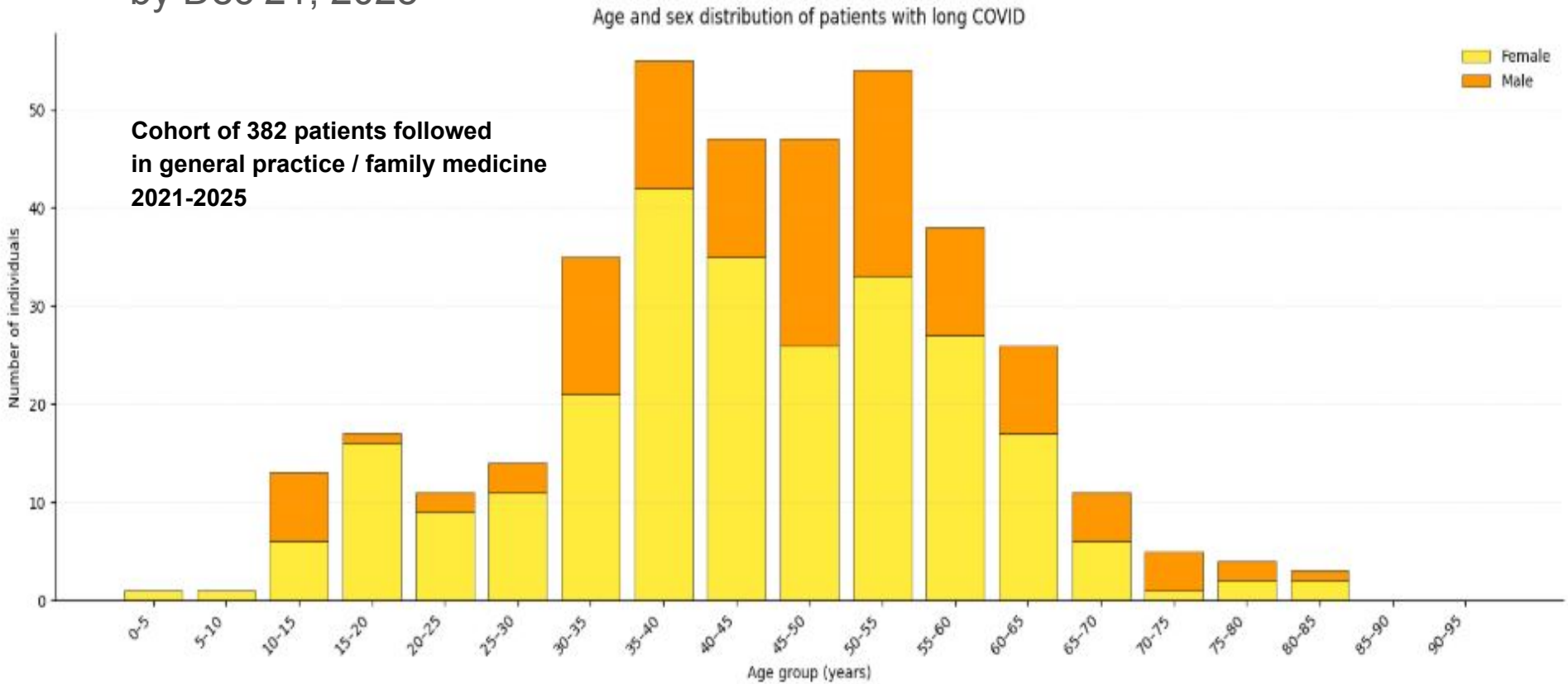


Figure X | Age and sex distribution of patients clinically affected by long COVID.
Stacked vertical histogram showing the distribution of patients by 5-year age groups (yellow: females; orange: males). Age was calculated as of **20 December 2025** based on date of birth. The study population comprised 382 patients, including 256 females (67.0%) and 126 males (33.0%)., with ages ranging from **7 to 85 years**. As for December 20, 2025 (M.Jamoulle, Charleroi, Belgium 2021-2025)

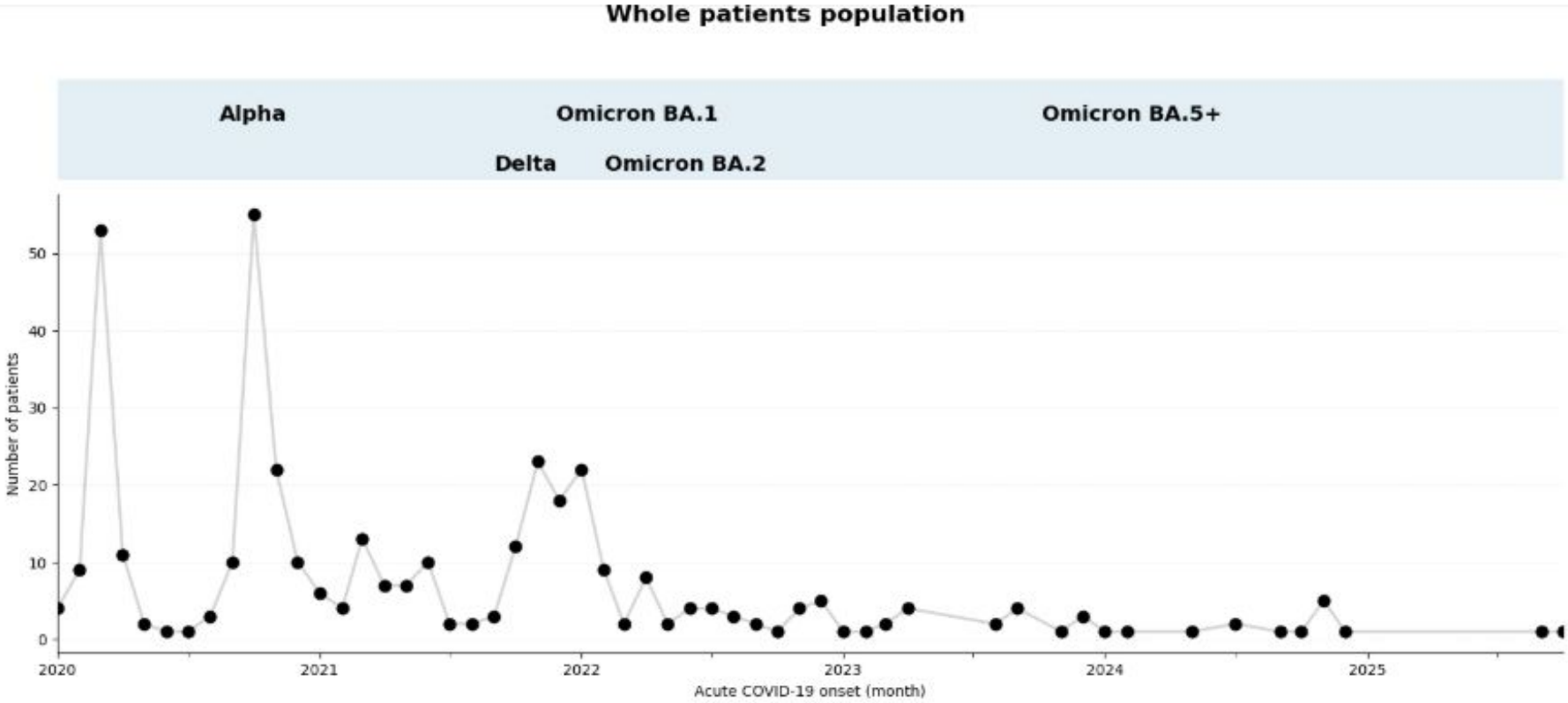


Figure X | Temporal distribution of acute COVID-19 onset in the whole patient population.
Monthly distribution of patients according to the date of acute SARS-CoV-2 infection (*first_covid_date*), with the x-axis starting in **January 2020**, corresponding to the onset of the COVID-19 pandemic. Black dots represent observed monthly counts, and the light grey line indicates temporal continuity. The upper timeline shows periods during which major SARS-CoV-2 variants were dominant in Belgium, based on **Sciensano** genomic surveillance data (Alpha, Delta, Omicron BA.1, BA.2, BA.5+). The study population comprised 382 patients, including 256 females (67.0%) and 126 males (33.0%)., with ages ranging from **7 to 85 years** as for December 20, 2025. (M.Jamoulle, Charleroi, Belgium 2021-2025)

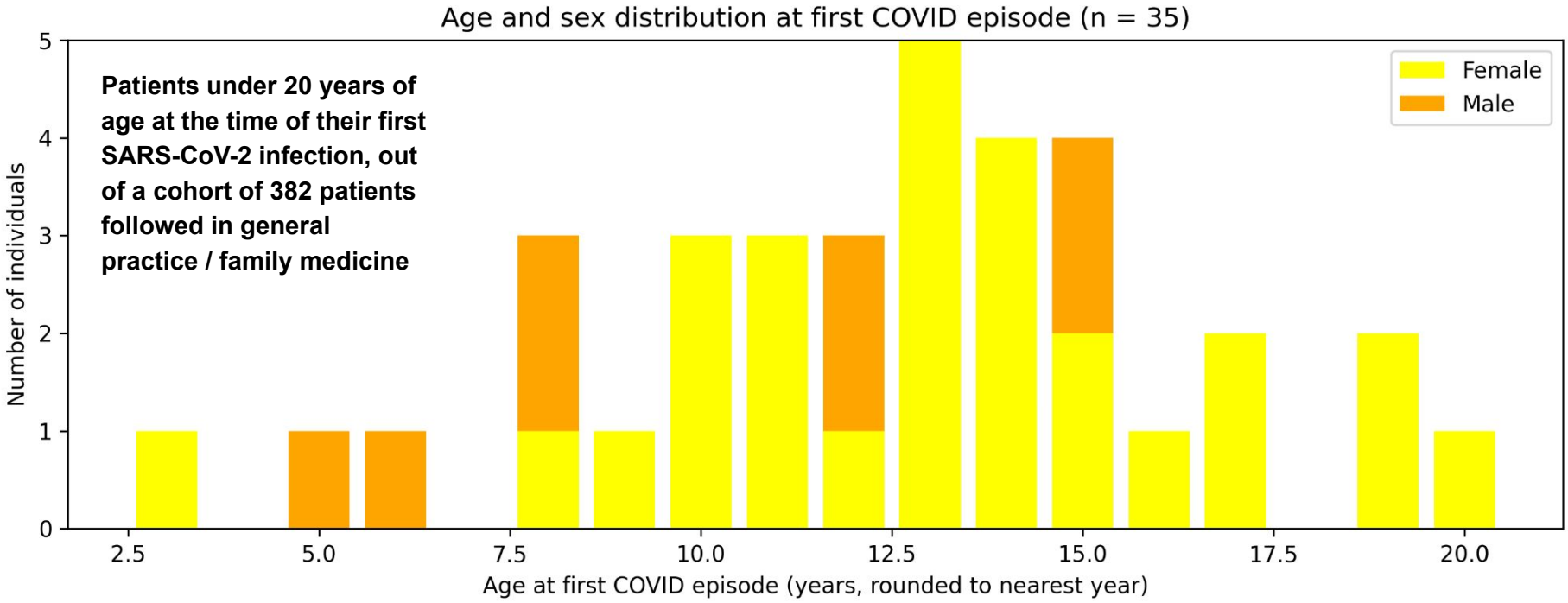
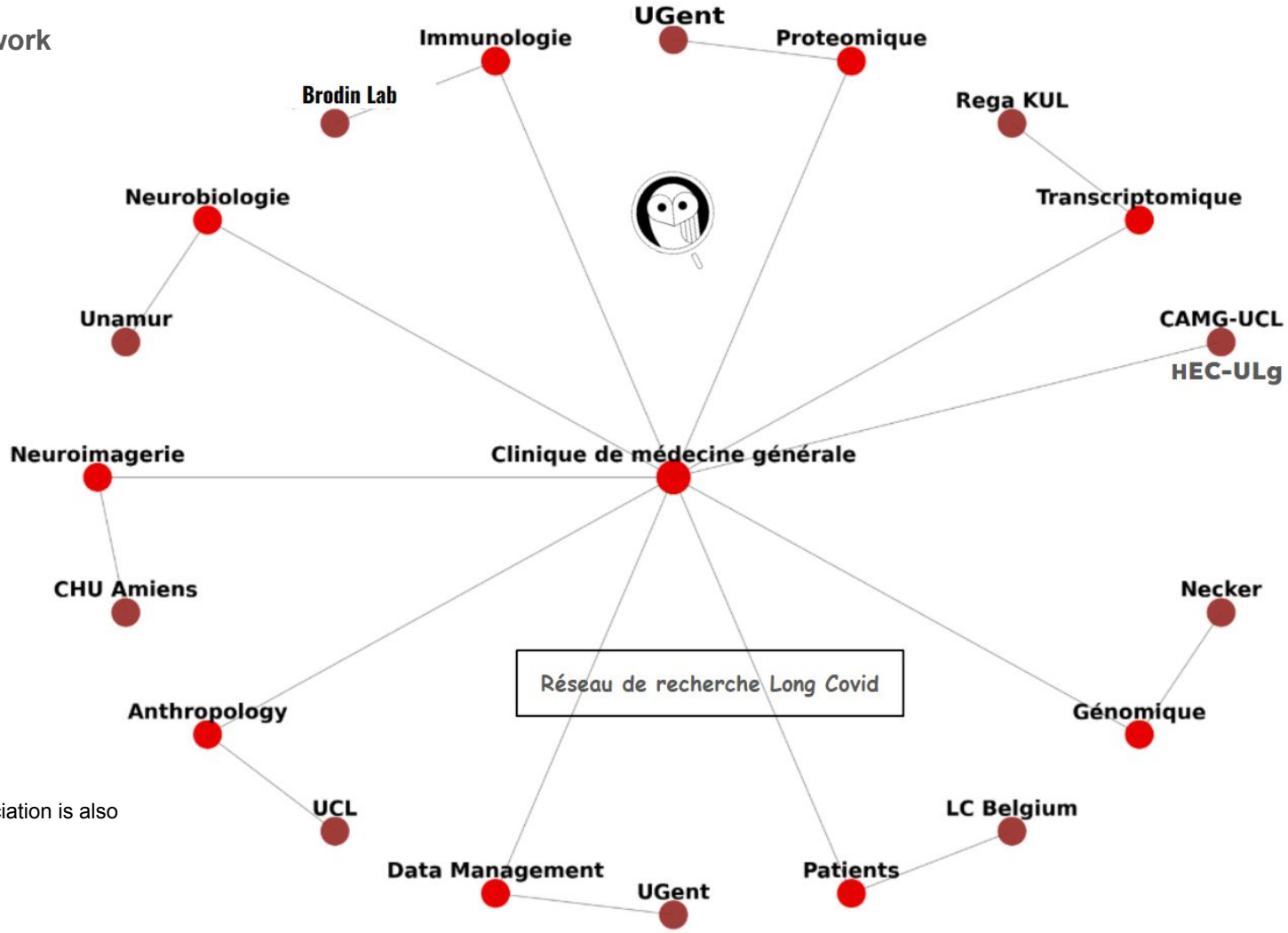


Figure Y. *Age and sex distribution at first COVID episode (20 years) in paediatric and adolescent Long COVID patients.*
Stacked bar chart of age at first documented COVID episode among **35 Long COVID patients followed in family practice**, including **27 females (77.1%)** and **8 males (22.9%)**, with ages ranging from **3 to 20 years**.
(Dr Jamoulle, Charleroi, Belgium, 2021–2025).

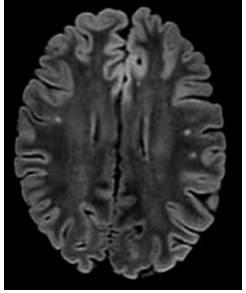
Long Covid Research Network

This research network emerged out of the blue, driven by the personal commitment of its participants

I will present the outcomes of the research conducted by this network, which operates on a voluntary basis without dedicated research funding.
I will begin with the current stage of the research.



The Belgian Long COVID patient association is also one branch of this network.

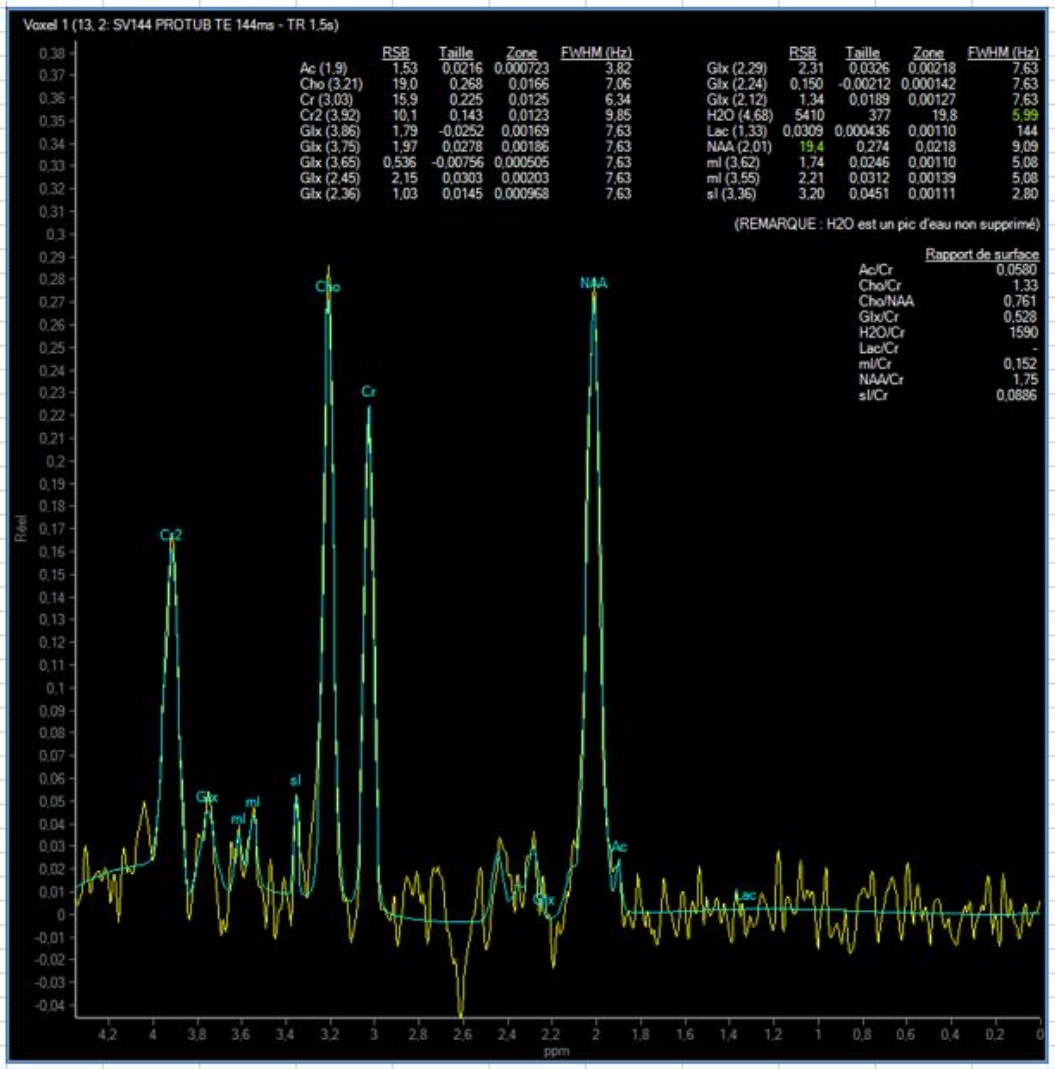


RMN; Three small hyperintense lesions, at the limit of normal findings

Magnetic resonance spectroscopy

Prof.Jean Marc Constans MD, PhD. Service de Neuro Radiologie et Imagerie Médicale,CHU Amiens, France

Boussida, Salem, et al. *Journal of Neuroradiology*, vol. 52, no. 2, Mar. 2025, p. 101282, https://doi.org/10.1016/j.neurad.2025.101282



Functional MR spectroscopy illustrating the main metabolic peaks observed (Cho, Cr, NAA, Lac, Glx).
Example of a Long COVID patient ;
onset of neuronal dysfunction and onset of inflammation in the pons

Comparative analysis of metabolic spectra from a patient with Long COVID for 3 years compared with control individuals.

Hypothesis of a chronic viral encephalitis, possibly attributable to SARS-CoV-2.

1. How did we come to request these imaging studies?
2. What are the stages of the action research process?
3. What research activities are currently underway at our level?
4. How are patients being supported?

- **Identification of a new syndrome**
- **Case record review / limited usefulness of standard laboratory tests and conventional imaging**
- **Literature review**
- **Data and indicator collection**
- **Search for alternative methods and additional partners**
    - **Technetium scintigraphy**
    - **MRS**
    - **Multi-omics approaches**
    - **Neurobiology**
    - **Virology**

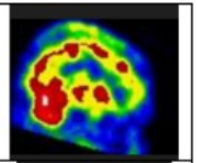
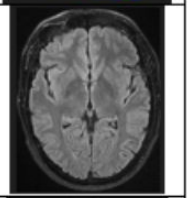
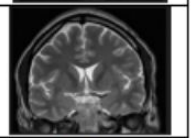
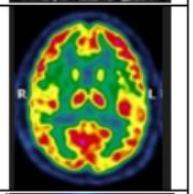
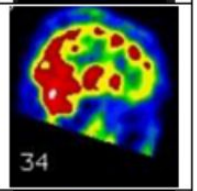
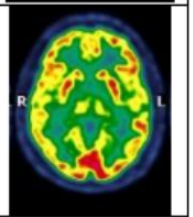
→ biblio; PubMed & Google Scholar watch since 2021 on Zotero

In search of the appropriate imaging modality

The choice of the imaging modality in 2021 had to account for the presumed vascular nature of Long COVID: PET evaluates neuronal metabolic activity, whereas technetium scintigraphy documents perfusion abnormalities, consistent with chronic endotheliitis.

Criterion	SPECT-CT (Technetium)	18F-FDG PET Scan
Tracer Used	Technetium-99m HMPAO [2]	Fluorodeoxyglucose (18F) [3]
Action	Absorbed by brain tissue in proportion to blood flow	Absorbed by brain tissue in proportion to glucose metabolism [4]
Target	Assess blood flow	Assess metabolism
Radiation Type	Emits gamma rays	Emits positrons
Irradiation Time	6-hour half-life	Longer body retention, about 2-hour half-life
Linear Energy Transfer (LET)	Lower	Higher [5]
Economic Cost	145 to 450 €	800 to 1,200 €
Environmental Cost	++	++++ [6]

Table 3.7 – Comparison between SPECT-CT (Technetium) and 18F-FDG PET Scan

SPECT CT 13th month	28/04/2021 Severe disturbance of cerebral vascular perfusion (very heterogeneous fixation throughout the cortex, area of marked hypofixation left fronto-parietal	
Brain MRI 16th month	05/07/2021 Normal caliber of the ventricular system. Trophycity and normal appearance of the hippocampi. No intracranial expansive process; No recent or sequential haemorrhagic lesion. Conclusion: negative examination	
Brain CT-Scan 16th month	06/07/2021 No structural abnormalities. Conclusion: negative examination	
18FDG PET-CT 16th month	29/07/2021 Discrete hypometabolism, not significant compared to a normal database, in the cerebral cortex in the superior parietal ans temporal areas, bilaterally. Conclusion: no formal argument for Alzheimer's dementia	
SPECT CT Control 27th month	23/06/2022 Heterogeneous tracer binding throughout the cerebral cortex, in the basal ganglia and in the thalamus. Normal and symmetrical binding in the cerebellum. Conclusion ; the scintigraphic aspect of the abnormalities rather pleads for a vascular origin	
18FDG PET-CT 29th month	04/08/2022 Compared to the examination of 29/07/2021, persistence of a discrete cortical hypometabolism in the right parieto-temporal brain right cerebral parieto-temporal hypometabolism not significant.	

Scintigraphy shows hypoperfusion

MRI: normal

Male, 50 years old
COVID-19 onset: 03/2020
Senior executive
5 years of total work incapacity

CT scan: normal

PET scan: normal

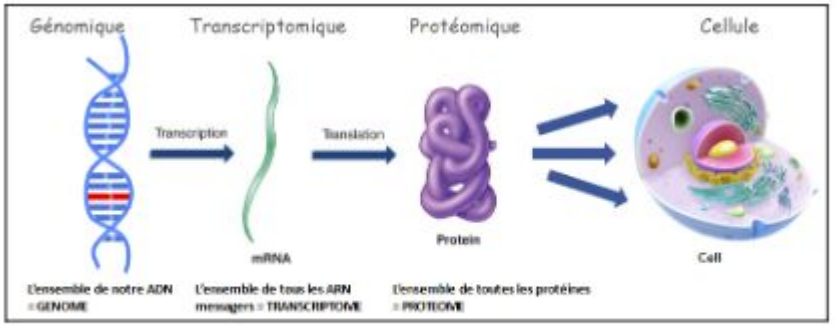
Scintigraphy: vascular perfusion abnormalities

PET scan: non-significant hypometabolism

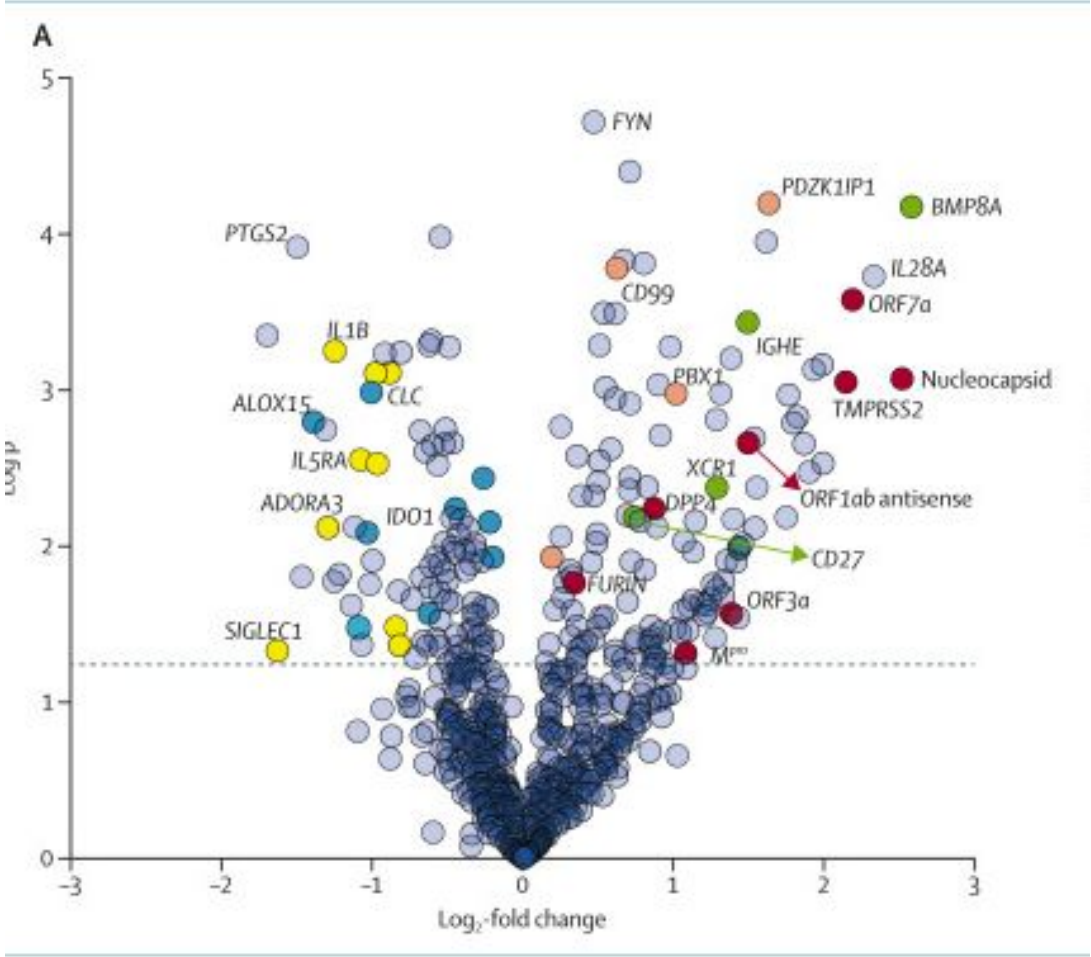
Jamoulle, M., et al (2022). *Viruses*, *14*(9), 2000.

Conventional cellular biology and imaging: non-contributory

- **Use of isotope-based imaging**
- **Use of functional MRI imaging**
- **Use of multi-omics biology and neurobiology**
  - Genomics
  - Transcriptomics
  - Proteomics
  - Immune profiling



Transcriptomic analysis of blood samples from 48 of my patients and 16 controls

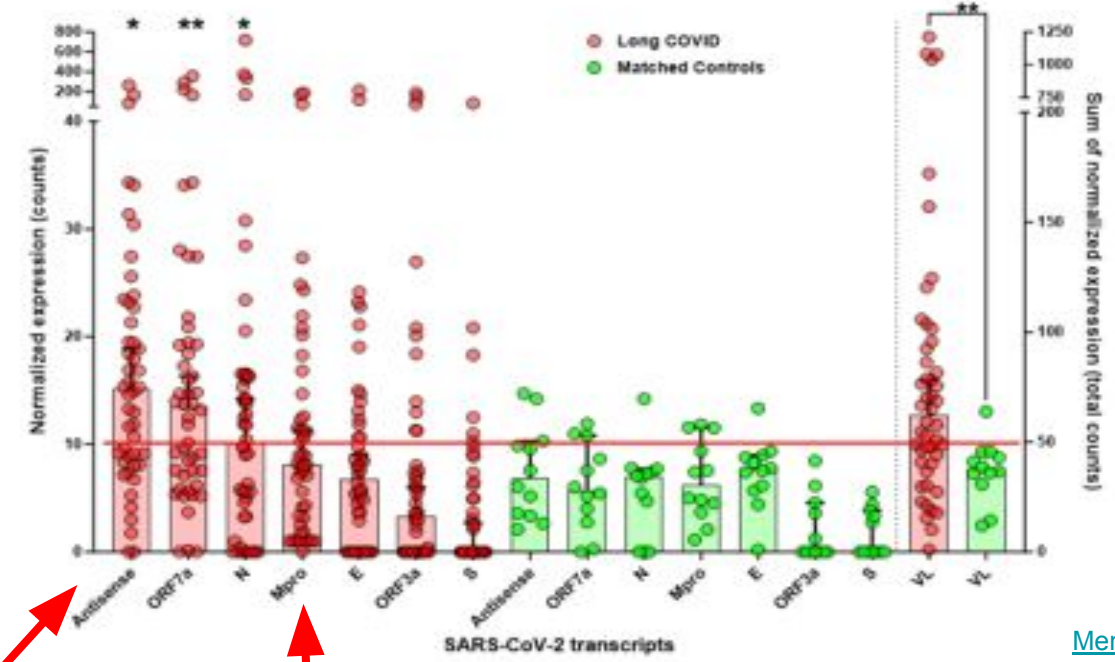


Johan Van Weyenberg, senior immunologist; Rega, KUL

The presence of ORF1ab antisense RNA and Mpro is only possible if the virus is viable.

Menezes, S. M., Jamoulle,et al (2024). *The Lancet Microbe*, *5*(8).

Results digital transcriptomics:
Long COVID (n=48) vs. controls (n=12)
Average 2 years after acute COVID



Long COVID patients:

- Higher Nucleocapsid, ORF7A, ORF3A, Mpro, Env RNA
- 65% antisense RNA+ : ongoing viral replication

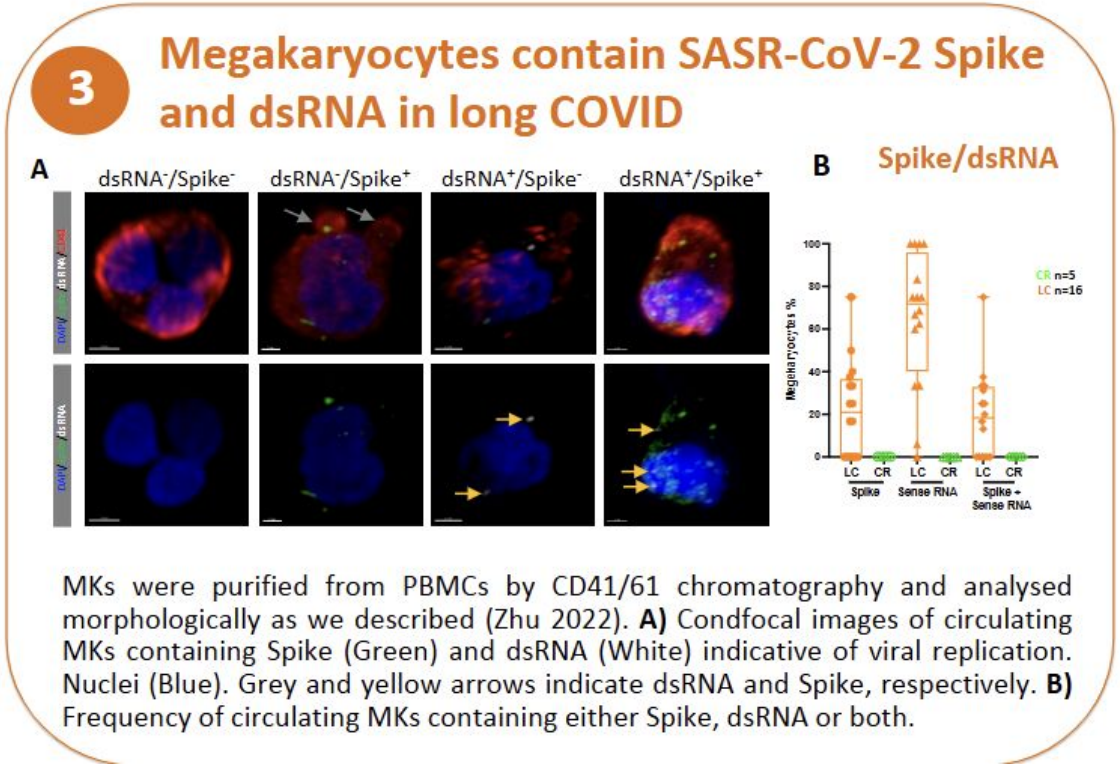
Compared to matched controls (age, sex, vaccination status, comorbidities, time since acute COVID-19)

Menezes, S. M., Jamoulle,et al (2024). *The Lancet Microbe*, *5*(8).

The emerging hypothesis is that the virus remains viable, with neurotropic and multisystemic properties.

Morgane Bomsel
Dominique Salmon
(Cochin Paris)

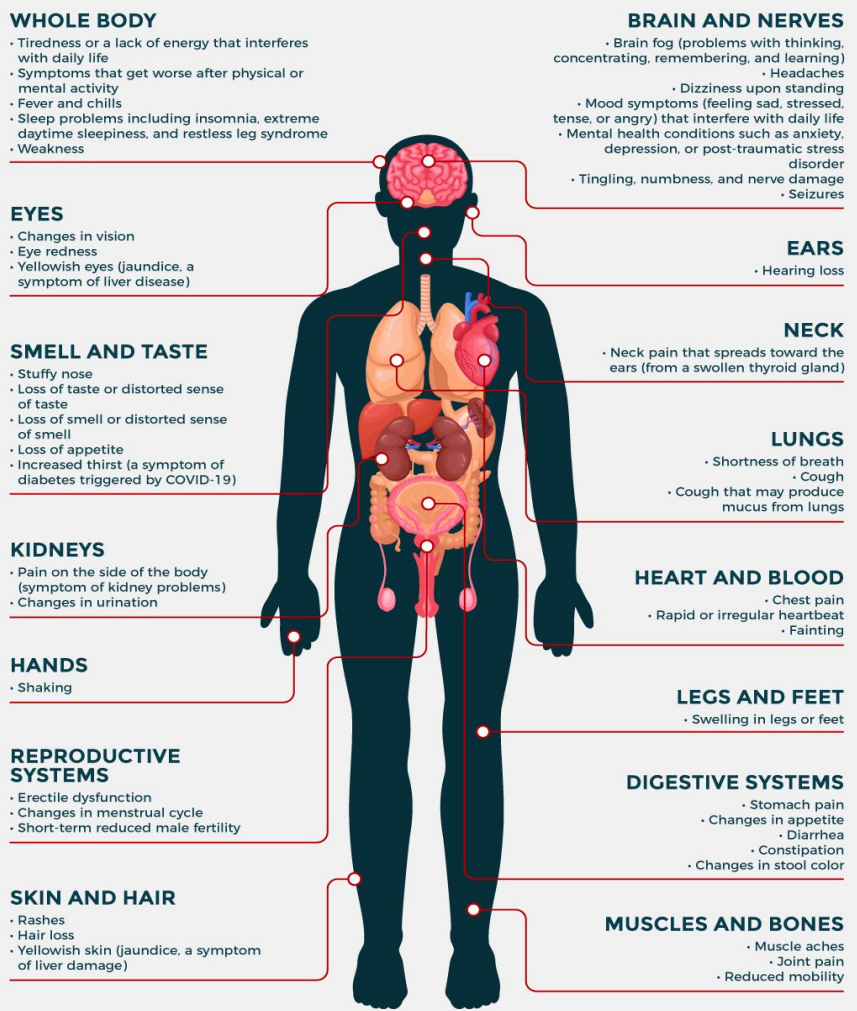
https://www.croiconference.org/wp-content/uploads/sites/2/posters/2024/347.pd



Chronic SARS-CoV-2 infection represents a new disease entity: complex, multisystemic, neurotropic, relapsing, disabling, and disruptive.

- **Female-to-male ratio: 2:1**
- **Patients grieving for their former selves**
- **Children withdrawn from school**
- **Adults on long-term sick leave**
- **Affects an estimated 5–10% of acute COVID cases**

MedShadow Foundation – *Symptoms of Long COVID Infographic* (2023)



Let us return to the starting point: the patient

The clinical approach
Hearing
2021

Figure 1. Patients' word bag. Word cloud extracted from verbatim statements of the first 34 patients seen in general practice in 2021. M. Jamoulle, consultation notes (English version).

Jamoulle, M., Kazeneza-Mugisha, G., & Zayane, A. (2022). Follow-up of a cohort of patients with post-acute COVID-19 syndrome in a Belgian family practice. *Viruses*, *14*(9), 2000. https://www.mdpi.com/1999-4915/14/9/2000

All patients with Long COVID share one common characteristic: loss.

Not always all losses at the same time, but loss nonetheless.

Loss of skills, loss of energy, loss of memory, loss of words, loss of balance, loss of taste and smell, loss of automatic regulation of the body's control systems, loss of sleep, and often loss of work.

Loss of social relationships, loss of libido, loss of couple relationships, loss of relationships with children, loss of their deeper self, and loss of trust in medicine.

The patient is the expert / Discovering the disease

I am so tired, I am no longer myself; I can't run anymore, I can't even walk fast.

I can no longer make any effort; I become immediately short of breath, as if my chest were being crushed.

I have such severe headaches; it feels like a leaden weight on my shoulders, radiating down my arm.

My leg moves on its own, my feet tingle and sometimes my hands; sometimes the pain shoots so intensely.

I get bruises that appear and disappear.

The clinical approach
Analyzing
using AI

patient + doctor +

Symptoms recording

automatic
transcription

https://www.vook.ai/

VookAI

LLM interpretation by HPO

https://chatgpt.com/

https://hpo.jax.org/

The Human Phenotype Ontology (HPO) is a standardized nomenclature of human clinical signs and symptoms, used here for diagnosis and research.

The clinical approach Analyzing using AI

General symptoms

Fatigue (HP:0012378); [I am so tired, I am no longer myself]

Respiratory / cardiovascular

Exercise intolerance (HP:0003546);[I can no longer make any effort; I become immediately short of breath]

Dyspnea (HP:0002094); [I become short of breath, as if my chest were being crushed]

Neurological

Headache (HP:0002315); [I have such severe headaches, like a leaden weight on my shoulders]

Radiating pain (HP:0002691);[It radiates down my arm]

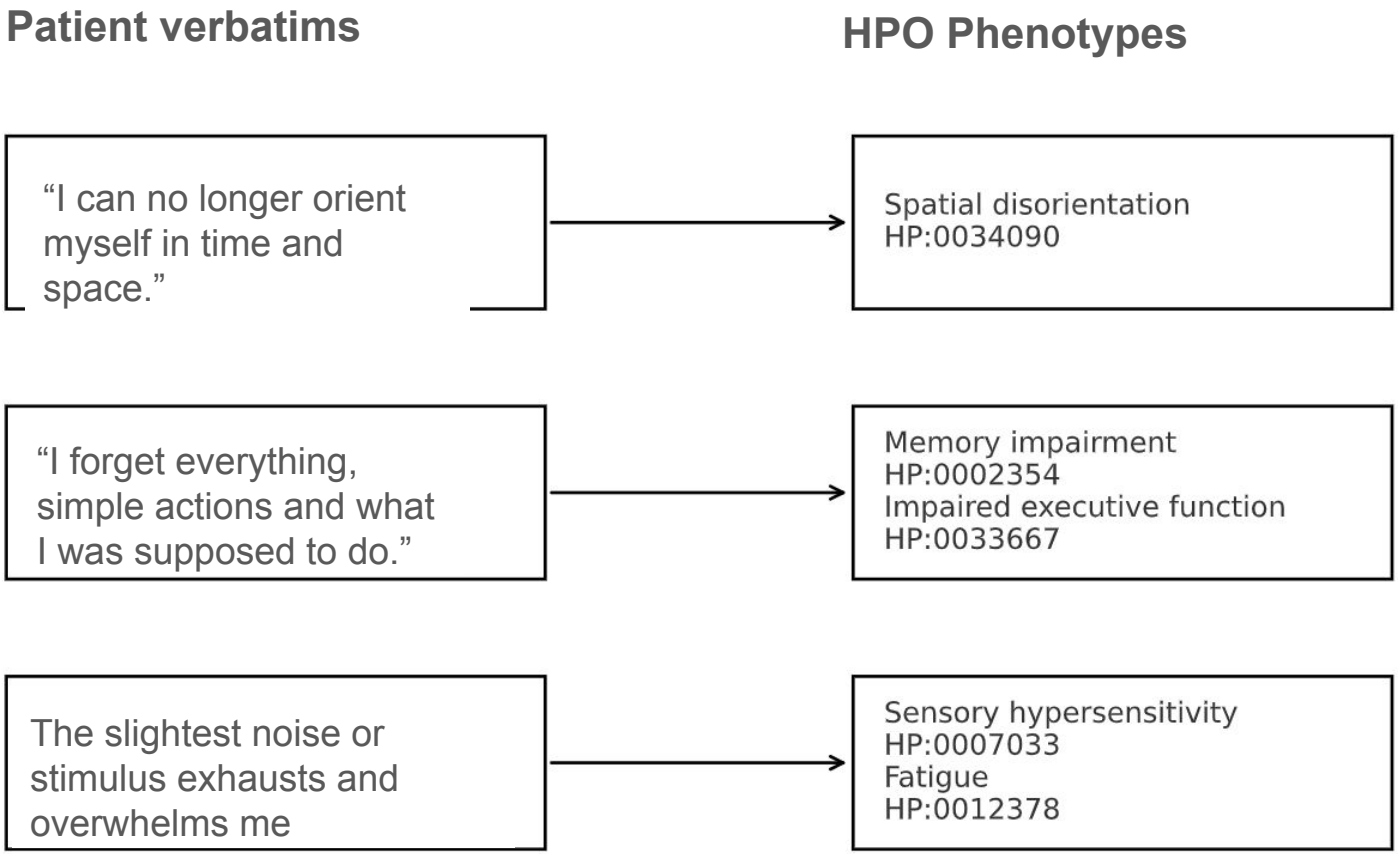
Involuntary movements (HP:0004305);[My leg moves on its own]

Paresthesia (HP:0003401); [My feet tingle and sometimes my hands]

Neuropathic pain (HP:6000040); [Sometimes the pain shoots intensely]

Dermatological / hematological

Ecchymosis (HP:0000978); [*I get bruises that appear and disappear"*



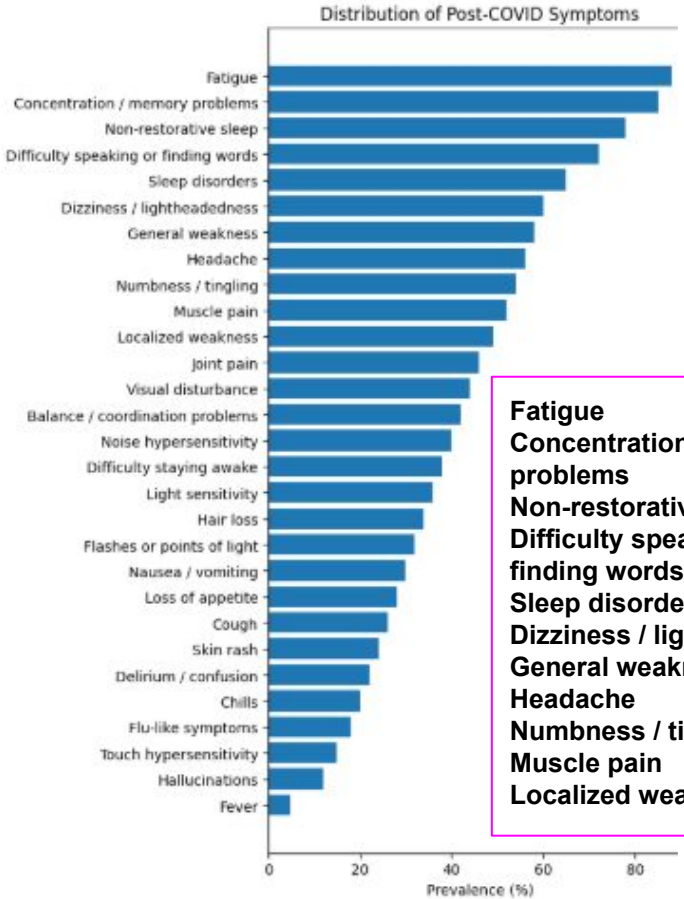
Construction of a terminological biomarker (LLM + HPO)

Each patients contribute with a set of coded verbatims

Huff, H. et all. (2025). *Frontiers in Neurology*, *16*, 1562084.

Australie

Doctor based

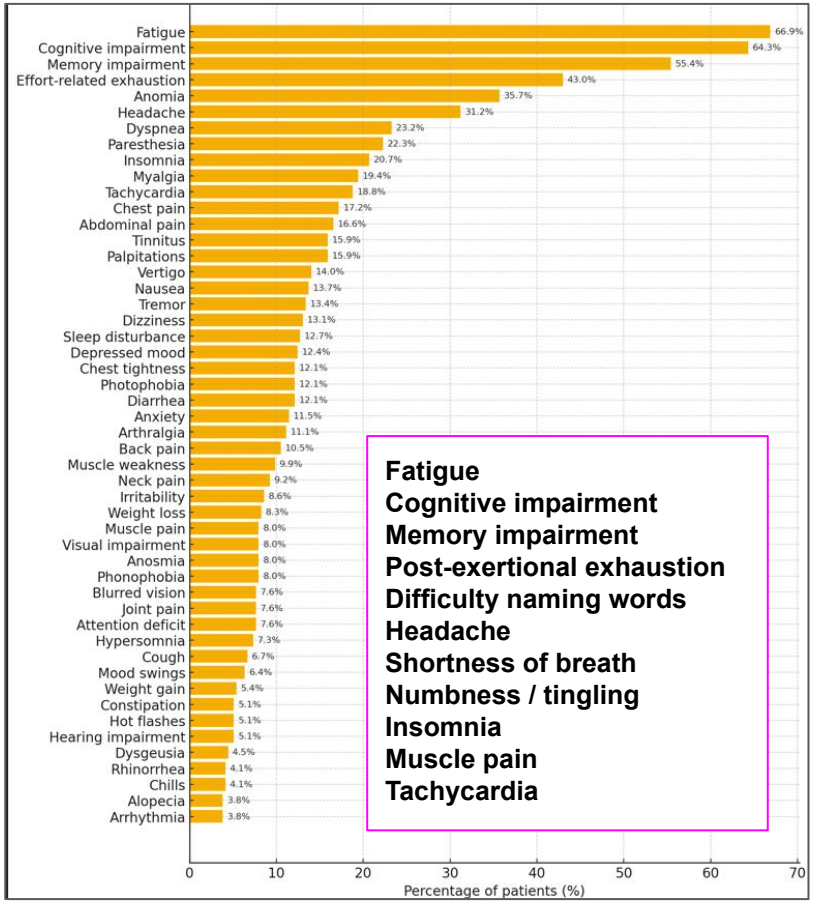


Fatigue
Concentration / memory problems
Non-restorative sleep
Difficulty speaking or finding words
Sleep disorders
Dizziness / lightheadedness
General weakness
Headache
Numbness / tingling
Muscle pain
Localized weakness

Prevalence of the verbatims of 307 patients / Charleroi / Belgium

Jamoulle Report 2021-2025

Patient based



Fatigue
Cognitive impairment
Memory impairment
Post-exertional exhaustion
Difficulty naming words
Headache
Shortness of breath
Numbness / tingling
Insomnia
Muscle pain
Tachycardia

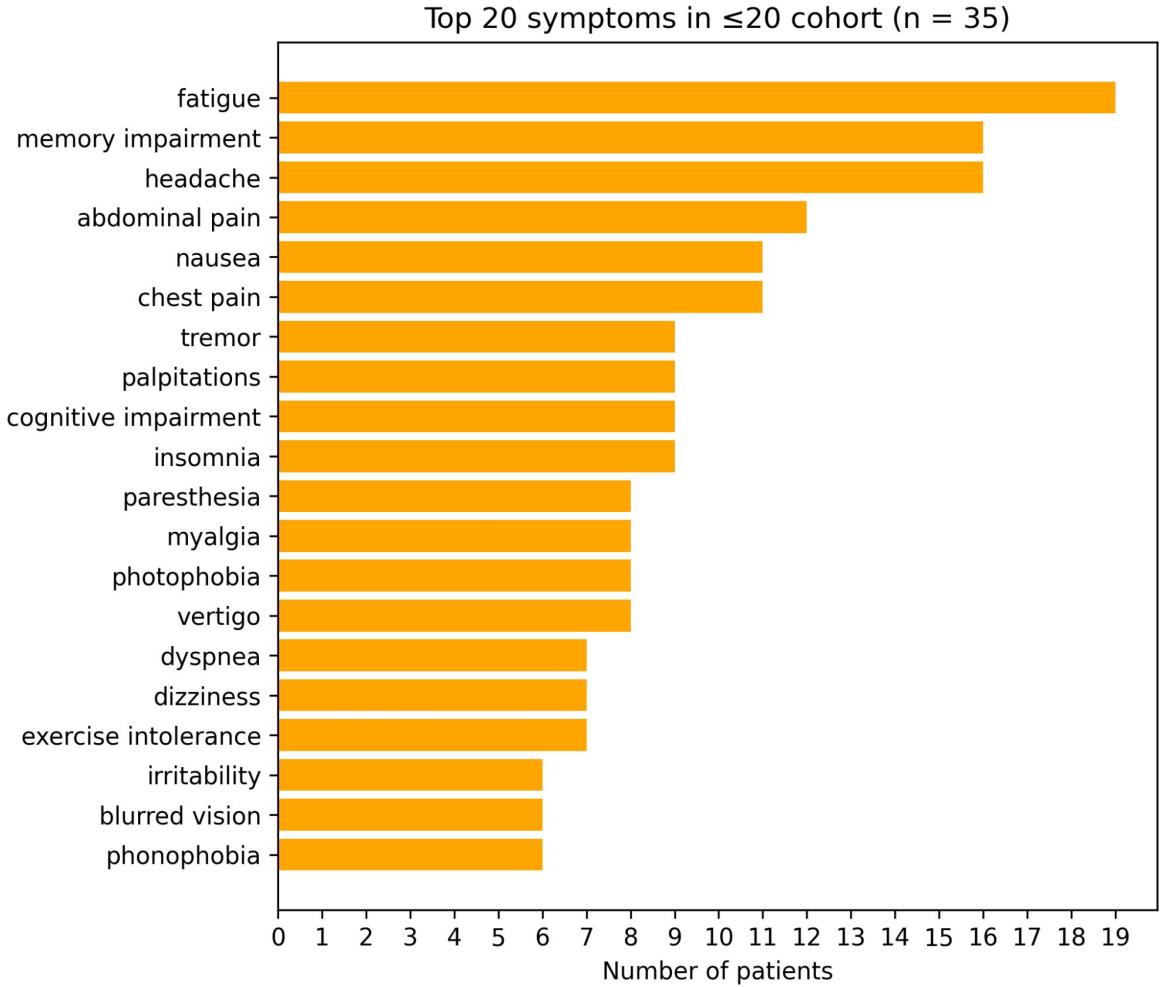


Figure X. *Top 20 symptoms in paediatric and adolescent Long COVID patients (≤ 20 years).*
Horizontal bar chart showing the 20 most frequently reported symptoms among patients who were ≤ 20 years of age at the time of acute SARS-CoV-2 infection, evaluated at their first family medicine consultation for suspected Long COVID. Symptoms were derived from semantic analysis of clinical descriptions, independent of HPO codes, and are expressed as the number of patients reporting each symptom.
(Dr Jamoulle, Family Medicine, Charleroi, Belgium, 2021–2025).

Where are we now?

- **No antiviral treatment currently available**
- **Multiple symptomatic treatments with variable and inconsistent outcomes**
  → literature review on potential therapeutic approaches
- **Medico-legal support is extremely challenging**
- **Psychological support and support for families are essential**
- **Facilitating connections with patient advocacy groups**
- **Ongoing research efforts** → several publications in progress
- **No dedicated funding; political and academic silence (at least in Belgium)**

Publication in progress

Epistemology: in partnership with patients (submitted)

The paradox of psychologizing Long COVID: when misattribution becomes a source of psychological harm

Martin Spanoghe[1,2,*], Tomaso Antonacci[1], Emilie Burel[1,3], Florence Herschke[1,3], Nicole Schneider[1,4], Thomas HJ Molmans[5,6], …, Marc Jamoulle[7]

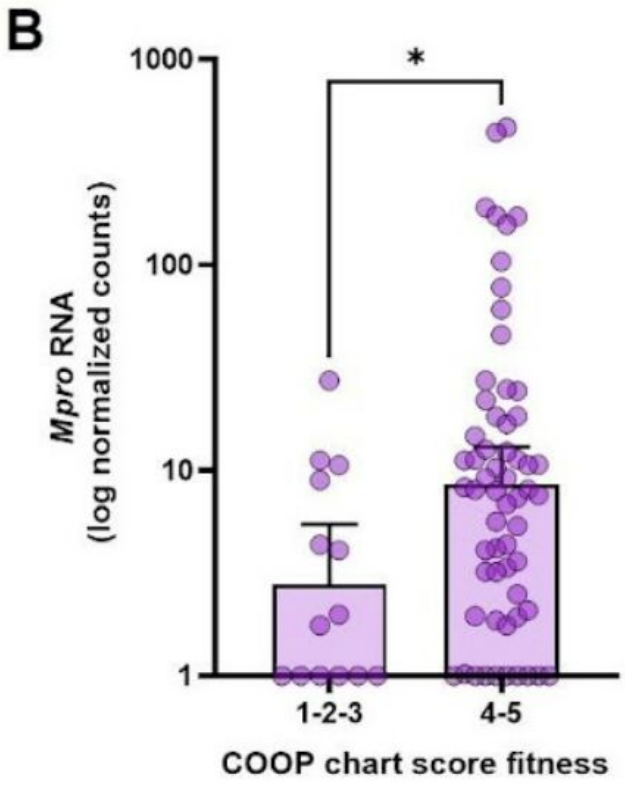
Publication in progress

Transcriptomic

SARS-CoV-2 Mpro protease as a biomarker and therapeutic target in Long COVID: a real-world prospective cohort study

The Lancet Microbe

Soraya Maria Menezes; Marc Jamoulle; Chen-Yu Liu; Elena Louazon; Tomaso Antonacci; Serhan Soylu; Daniel Sanson; Leen Moens; Margaux Mignolet; Aurélie Ladang; Charles Nicaise; Bart Van Puyvelde; Maarten Dhaenens; Isabelle Meyts; Kathleen Freson; Petter Brodin; Johan Van Weyenbergh



Publication in progress

Preprint Neurobiologie ; Charles Nicaise UNamur

Pathogenic IgG from long COVID patients with neurological sequelae triggers sensitive but not cognitive impairments upon transfer into mice

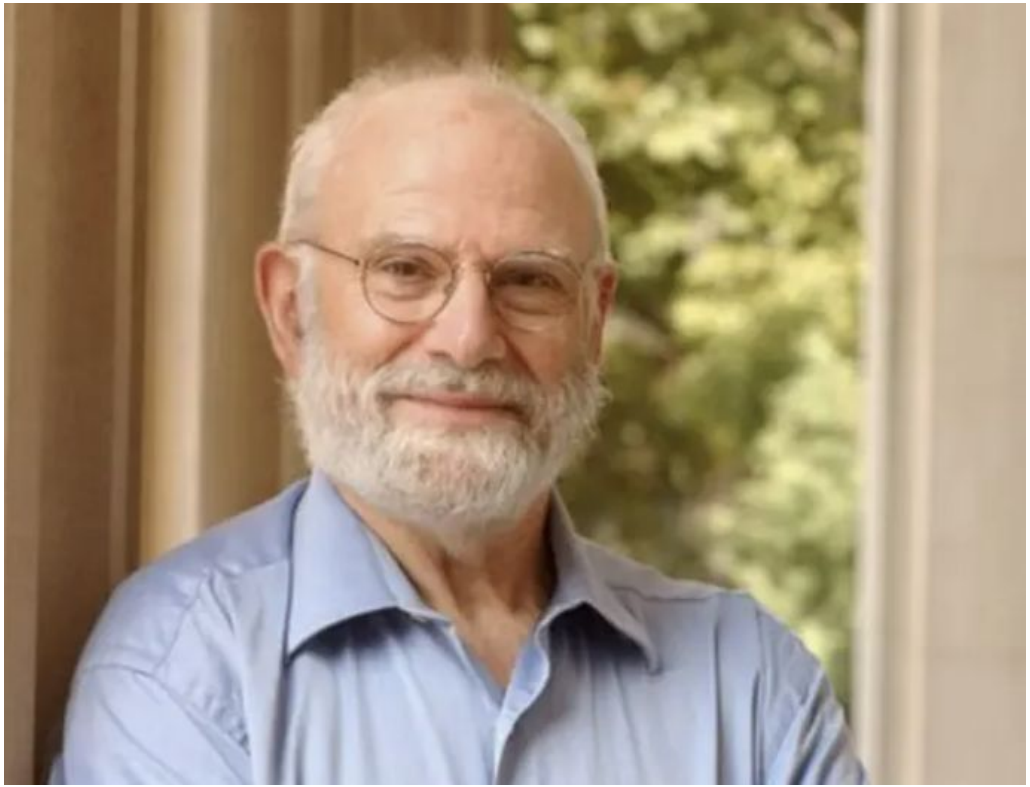
Margaux Mignolet, Catherine Deroux, Thomas Florkin, Valéry Bielarz, Kathleen De Swert, Nicolas Halloin, Lindsay Sprimont, Aurélie Ladang, Fabienne George, Jacques Gilloteaux, Laurence Abeloos, Johan Van Weyenbergh, Marc Jamoulle, Claire Diederich, Nicolas Albert Gillet, Pierre Bulpa, Charles Nicaise

doi: https://doi.org/10.1101/2025.11.20.689423

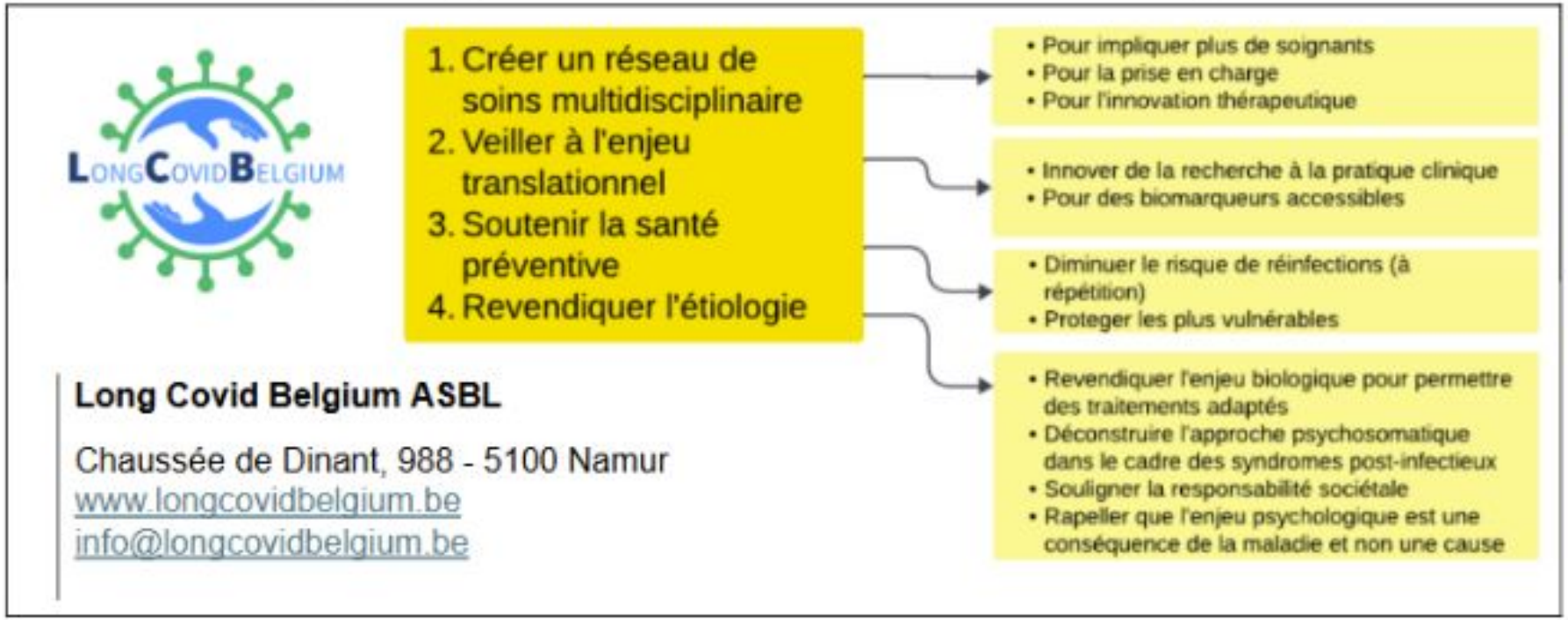
So, if the course of a patient's life has changed dramatically…

- Do not label the patient — listen to them.
- Take the time to list all symptoms,
- starting with life impact and brain functions,
- then all bodily systems and pain.
- Write down or record everything the patient says. He/she is the expert
- A clear memory of acute COVID is not required.
- Vaccinated or not.
- If 4 or 5 symptoms from the list above are present, consider the hypothesis of Long COVID.
- Be cautious: the patient is grieving for their former self.

To restore the human subject to the center — the suffering subject, the afflicted subject, the struggling subject, the human subject — we must deepen a case history into a narrative.”
Oliver Sacks, The Man Who Mistook His Wife for a Hat

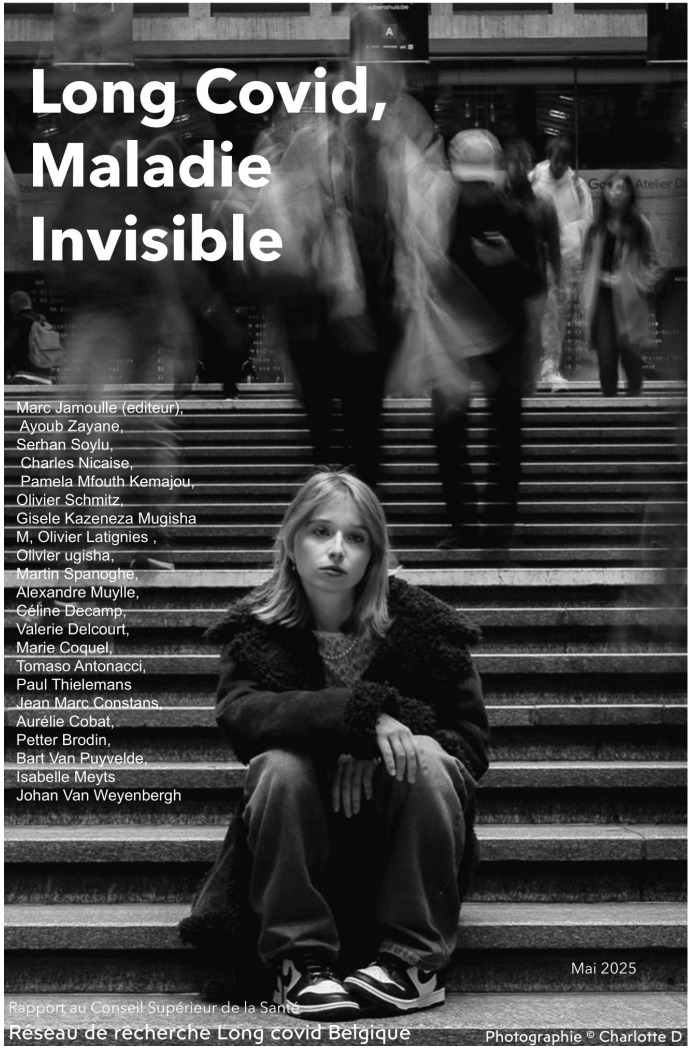


Importance of patient associations



xFigure 4: . Cible stratégique de l'association de patients Log Covid Belgium (https://longcovidbelgium.be)

Jamoulle, M.; Réseau de Recherche Long Covid Belgique. Long COVID: Invisible Illness. Technical report, 2025. 712 https://orbi.uliege.be/handle/2268/335655



emji2025