Wonca WICC Annual Meeting
Newcastle upon Tyne, UK
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Long Covid, invisible disease

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On behalf of the
Belgian Long Covid
Research Network
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Death and the Masks J.Ensor 1897

change of live

A pattern of unusual symptoms and two main determinants

loss of self

- **Fatigue** (HPO: HP:0012378)
- **Headache** (HPO: HP:0002315)
- **Muscle weakness** (HPO: HP:0001324)
- **Difficulty concentrating** (HPO: HP:0100543)
- **Short-term memory loss** (HPO: HP:000235
- **Dyspnea (difficulty breathing)** (HPO: HP:0002094)
- **Chest pain** (HPO: HP:0100749)
- **Leg pain** (HPO: HP:0002378)
- **Musculoskeletal pain** (HPO: HP:0003326)
- **Cognitive impairment** (HPO: HP:0100543)
- **Sleep disturbances** (HPO: HP:0031608)
- **Anxiety** (HPO: HP:0000739)

- **Cold extremities** (HPO: HP:0003703)
- **Hypersensitivity to pain** (HPO: HP:0033211)
- **Bruising** (HPO: HP:0000978)
- **Tachypnea (rapid breathing)** (HPO: HP:0002789)
- **Reduced ability to perform daily activities** (HPO: HP:0007349)
- **Impaired sense of smell (anosmia)** (HPO: HP:0000458)
- **Impaired sense of taste (ageusia)** (HPO: HP:0012724)
- **Gastrointestinal discomfort (bloating)** (HPO: HP:0003279)
- **Menstrual irregularities** (HPO: HP:0000858)
- **Sexual dysfunction** (HPO: HP:0000137)
- **Joint pain** (HPO: HP:0002829)

Sept 2024. Consultation ; Recording of a 10 min.conversation with a 36 year old woman, mother of two, third year of LC; detailed list of symptoms mentioned, mapped with their corresponding Human Phenotype Ontology (HPO) labels by a Language Model (ChatGPT4o) HPO codes not controlled

→ Those associations of symptoms does not correspond to either the patient's or the doctor's cultural context.

poor communication, relationship not established, patient does not feel understood, doctor frustrated

About Long COVID patients

All these patients share a common characteristic: the loss. Not often all in the meantime but loss. Loss of competence, loss of energy, loss of memory, loss of speech, loss of balance, loss of taste, loss of smell, loss of automatic regulation of the body's control systems, loss of sleep, often loss of work. Loss of social relationships, loss of libido, loss of relationships with children, loss of their deepest self and loss of confidence in medicine. They are in mourning for themselves and, because their serotonin is low, they are also losing their sense of struggle. Doctors, who don't take the time to listen or hear what they have to say, step into the breach and make unfounded diagnoses such as burnout or depression.

Research is advancing and we know that we are dealing with an illness of unknown complexity. There is no longer any doubt about the persistence of the virus, which attacks at several levels, through endothelial damage, the creation of autoantibodies, mast cell and platelet stimulation, and direct damage to the intestines. All this is in addition to the sequelae of the original infection. The most incredible scientific challenge I have ever faced.

Marc Jamoulle Family doctor from 1974

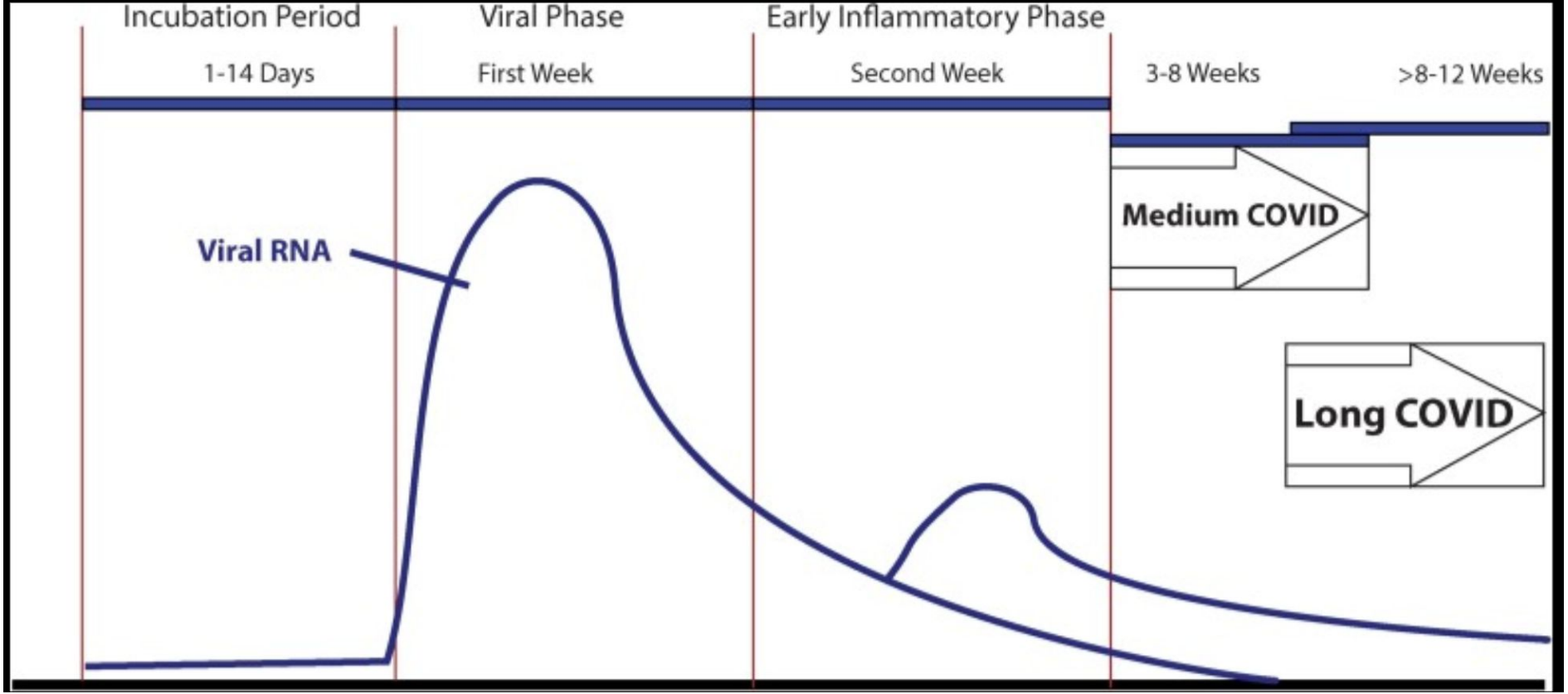
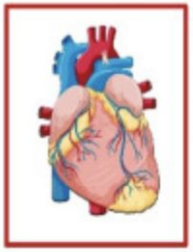


Figure 1. The stages of COVID-19: the incubation period, early inflammatory phase, delayed recovery period (medium COVID phase), and long COVID phase. Abbreviation: COVID-19, coronavirus disease 2019.

Griffin DO. Postacute Sequelae of COVID (PASC or Long COVID): An Evidenced-Based Approach. *Open Forum Infect Dis*. 2024;11(9):ofae462. doi:10.1093/ofid/ofae462



Cardiovascular

- Myocarditis
- Arrhythmias
- Acute myocardial infarction
- Chemical/non-ischemic cardiovascular illness
- Pericarditis
- Heart failure
- Thrombotic conditions

Respiratory System

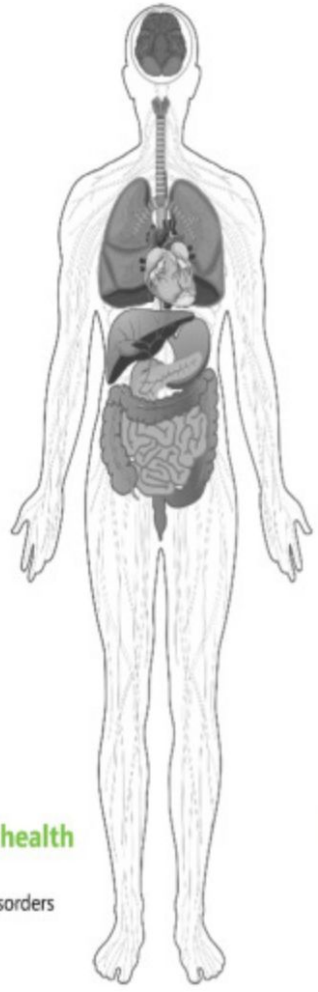
- Shortness of breath
- Cough
- Wheezing
- Reduced lung capacity
- Pulmonary fibrosis

Gastrointestinal

- Nausea
- Vomiting
- Abdominal pain
- Anorexia
- Diarrhea
- G.I. bleeding
- Acid reflux
- Constipation

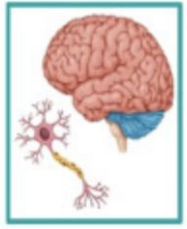
Mental health

- Anxiety
- Mood disorders



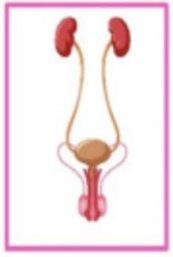
Metabolic/Endocrine

- Hyperglycemia
- Obesity
- Diabetes
- High cholesterol
- Hypothyroidism
- Hyperthyroidism,
- Adrenal insufficiency



Nervous System

- Headaches
- Confusion
- Delirium
- Encephalopathy
- Strokes
- Postural orthostatic tachycardia syndrome



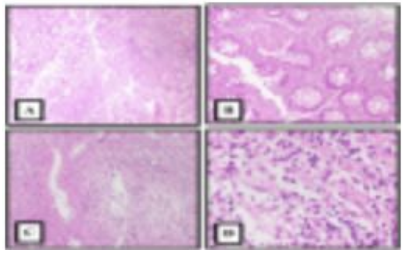
Genitourinary

- Orchitis
- Epididymitis
- Acute kidney injury
- Chronic kidney disease

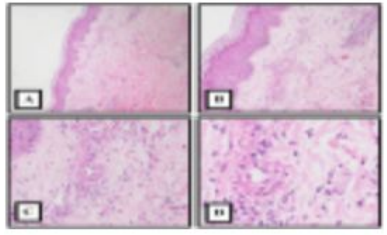
Musculoskeletal

- Myositis
- Arthritis
- Muscle weakness

Umakanthan, S.,et al (2024). Post-Acute Sequelae of Covid-19. *American Journal of Medicine Open*, *12*, 100071.



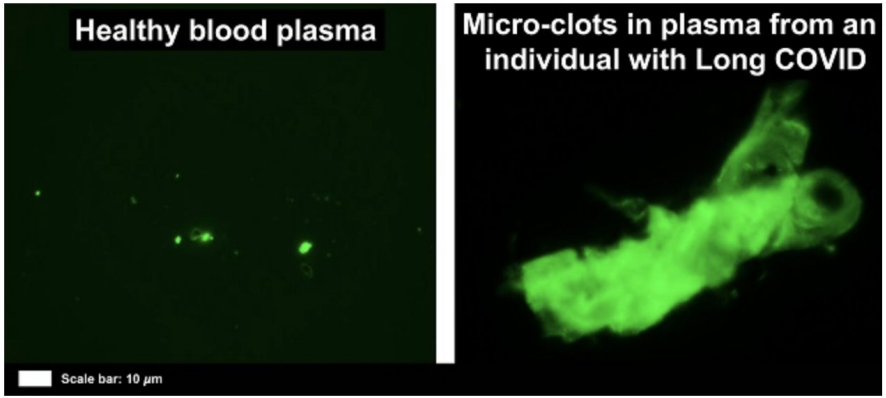
Microscopic images of Inflammatory bowel disease appearance in a patient with post COVID-19.



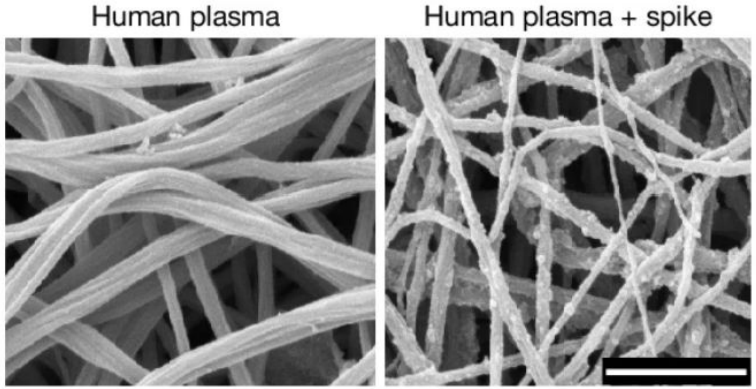
images demonstrating vasculitis in a patient with musculoskeletal features.

“...failure in the fibrinolytic process during COVID-19 and also in patients with lingering Long COVID/PASC symptoms. Our results show that plasma proteins in both COVID-19 and Long COVID/PASC plasma samples are greatly resistant to breakdown in the presence of trypsin””.

Pretorius E, Vlok M, Venter C, et al. Persistent clotting protein pathology in Long COVID/Post-Acute Sequelae of COVID-19 (PASC) is accompanied by increased levels of antiplasmin. *Cardiovasc Diabetol*. 2021;20:172. doi:10.1186/s12933-021-01359-7



Fibrin drives thromboinflammation and neuropathology in COVID-19

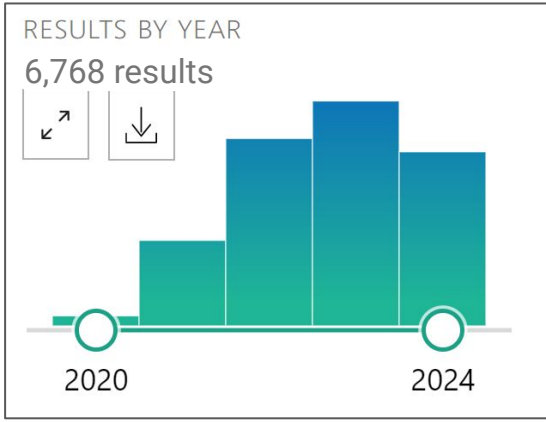


“ Our findings suggest that fibrin promotes neuropathological alterations either indirectly by inducing hyperinflammation through modulation of NK cells and macrophages in the infected lung or directly on microglia, owing to its parenchymal deposition in the brain “

Ryu JK, Yan Z, Montano M, et al. Fibrin drives thromboinflammation and neuropathology in COVID-19. *Nature*. August 2024:1-9. doi:10.1038/s41586-024-07873-4

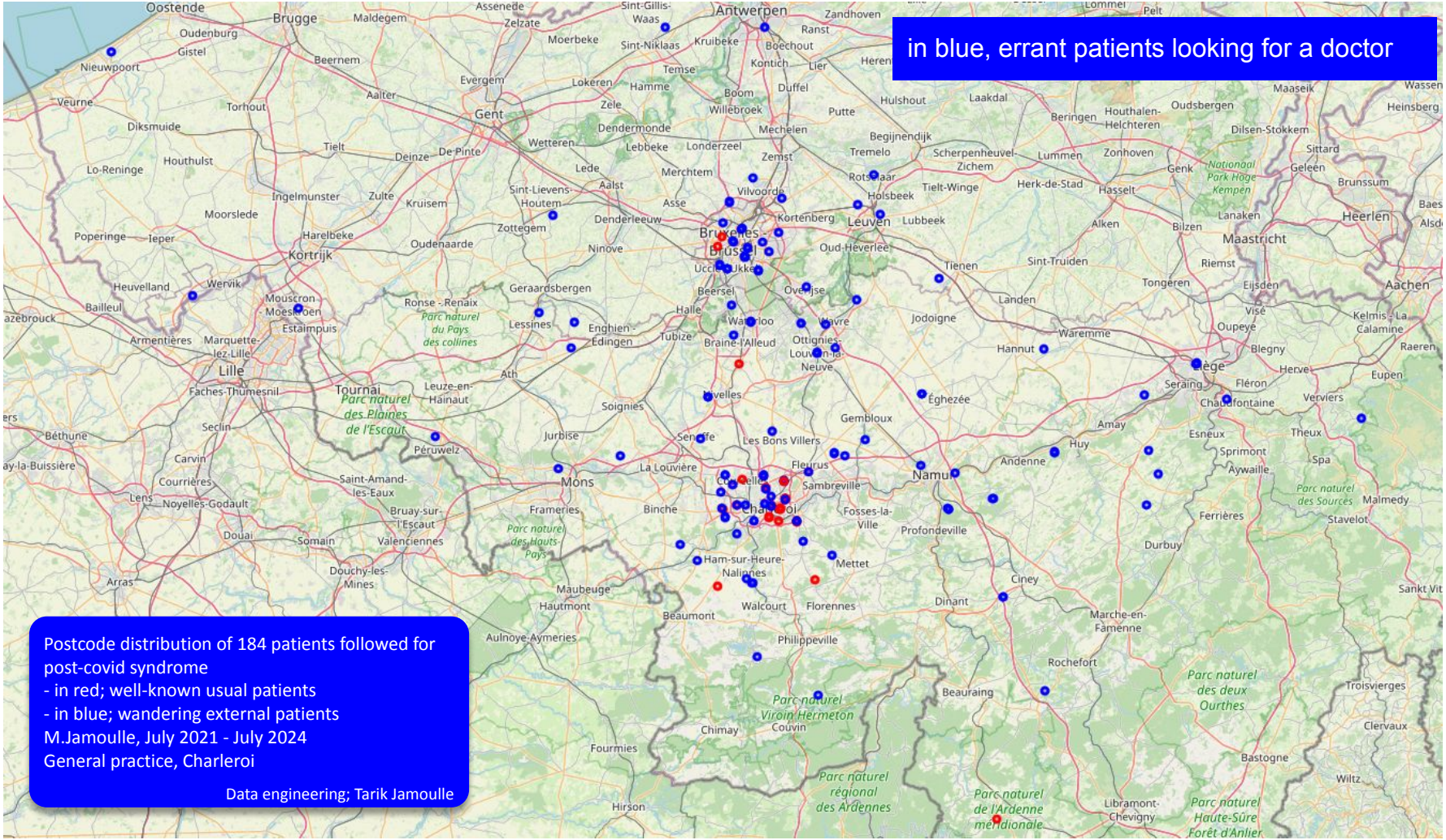
- Long Covid Open Library
  - CSF/ME
  - LC - publications MJ
  - LC - QR325 intervention study
  - LC-28 (Disability)
  - LC-33 (immunol.)
  - LC-37 anapath
  - LC-41(imaging)
  - LC-44 (vaccine)
  - LC-50 (therapeutics)
  - LC-51 (Phys.Revalidation)
  - LC-58 (Cogn revalidation)
  - LC-A (gen)
  - LC-B (bood)
  - LC-D (Dig)
  - LC-F (eye)
  - LC-H (ear)
  - LC-K (Circul)
  - LC-L(Osteoart)
  - LC-N (neuro)
  - LC-N (neuro)
  - LC-P (Psycho)
  - LC-QC12(child)
  - LC-QD23 (Health educ.)
  - LC-QD321(MUS)
  - LC-QD41 (prev I)
  - LC-QH1(envirr.)
  - LC-QP24 affordability
  - LC-QR 1(epistemo)
  - LC-QR2(epidemio)
  - LC-QR31 (quali)
  - LC-QR33 (mixte)
  - LC-QR4 (research network)
  - LC-QR51 (Class.)
  - LC-QR52(scale)
  - LC-QS13 (HIS)
  - LC-QS33 (Coordination)
  - LC-QT32 (guidelines)
  - LC-R (Respir)
  - LC-S (Skin)
  - LC-T (metab)
  - LC-U
  - LC-W (Pregnancy)
  - LC-X (Female)
  - LC-X (Male)
  - LC-Z (Social)

"Post-Acute COVID-19 Syndrome"[Mesh] or "Long Covid"[tw]



Sars-Cov-2 bibliography classified along ICPC-2 and some Q-codes

https://www.zotero.org/groups/4929325/long_covid_open_library/library


in blue, errant patients looking for a doctor
Postcode distribution of 184 patients followed for post-covid syndrome
- in red; well-known usual patients
- in blue; wandering external patients
M.Jamoulle, July 2021 - July 2024
General practice, Charleroi
Data engineering; Tarik Jamoulle

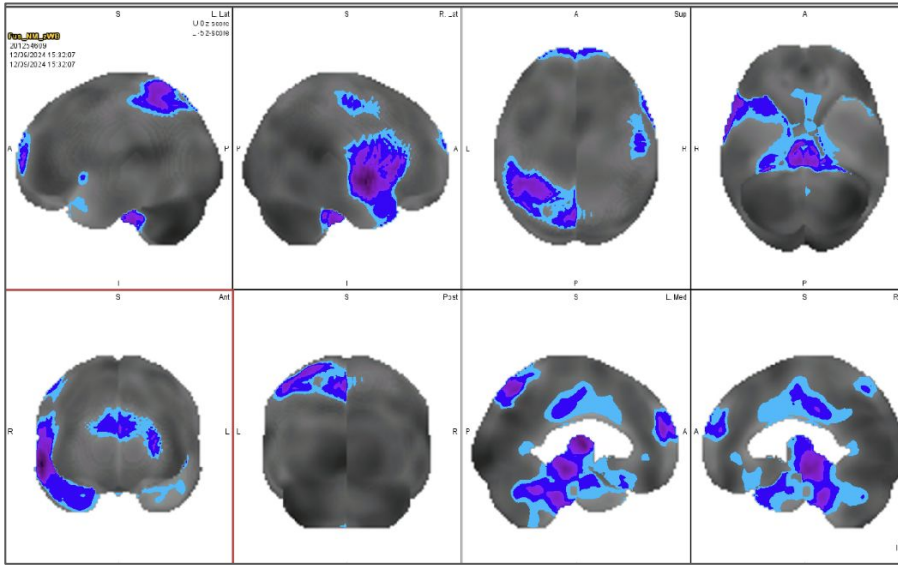
50 years old - Male - architect, off work for two years, labelled burnout

@jamoulle 2024

1. **Chronic fatigue**
   - HPO Code: **HP:0012378** (Chronic fatigue)
2. **Cognitive impairment**
   - HPO Code: **HP:0100543** (Cognitive impairment)
3. **Memory problems**
   - HPO Code: **HP:0002354** (Impaired memory)
4. **Shortness of breath**
   - HPO Code: **HP:0002094** (Dyspnea on exertion)
5. **Hyperventilation and chest tightness**
   - HPO Code: **HP:0002883** (Hyperventilation)
   - HPO Code: **HP:0002793** (Chest tightness)
6. **Dizziness**
   - HPO Code: **HP:0002321** (Dizziness)
7. **Erectile dysfunction**
   - HPO Code: **HP:0003251** (Erectile dysfunction)
8. **Decreased vision**
   - HPO Code: **HP:0000642** (Decreased visual acuity)
   - HPO Code: **HP:0000486** (Astigmatism)
   - HPO Code: **HP:0000540** (Hypermetropia)
9. **Sensory and dermatological symptoms**
   - HPO Code: **HP:0000486** (Astigmatism)
   - HPO Code: **HP:0009830** (Tingling)
   - HPO Code: **HP:0000955** (Skin desquamation)

Covid-19 infections: at least 4
First infection: September 2020 (not confirmed by PCR).
Subsequent infections : December 2022, November 2023, May 2024.
Covid-19 vaccination: Vaccinated, with no significant systemic or local reaction.

Brain
SPECT-CT
Blue = hypoperfusion



Moderate perfusion abnormalities of the right temporal pole, the left insular region, the thalami and the brainstem.These abnormalities could possibly be part of a long neurological covid with predominantly dysautonomic and cognitive-behavioural symptoms.
(3D-SSP de MIM Software. courtesy ; Prof. Hambye, Brugmann, Brussels)

all symptoms unknown before 2020

DUSOI: 4
COOP; 23/30

Biology normal but

SEROLOGIE VIRALE	
Epstein-Barr	
EBV IgG (VCA)	> 750,0
Herpès simplex (I+II)	
Herpès I+II IgG	Négatif
Varicelle	
VZV IgM	Négatif
VZV IgG	2396
Divers	
SARS-CoV-2 (Spike) IgG	> 2080 [a]

< 1990 ME/CSF

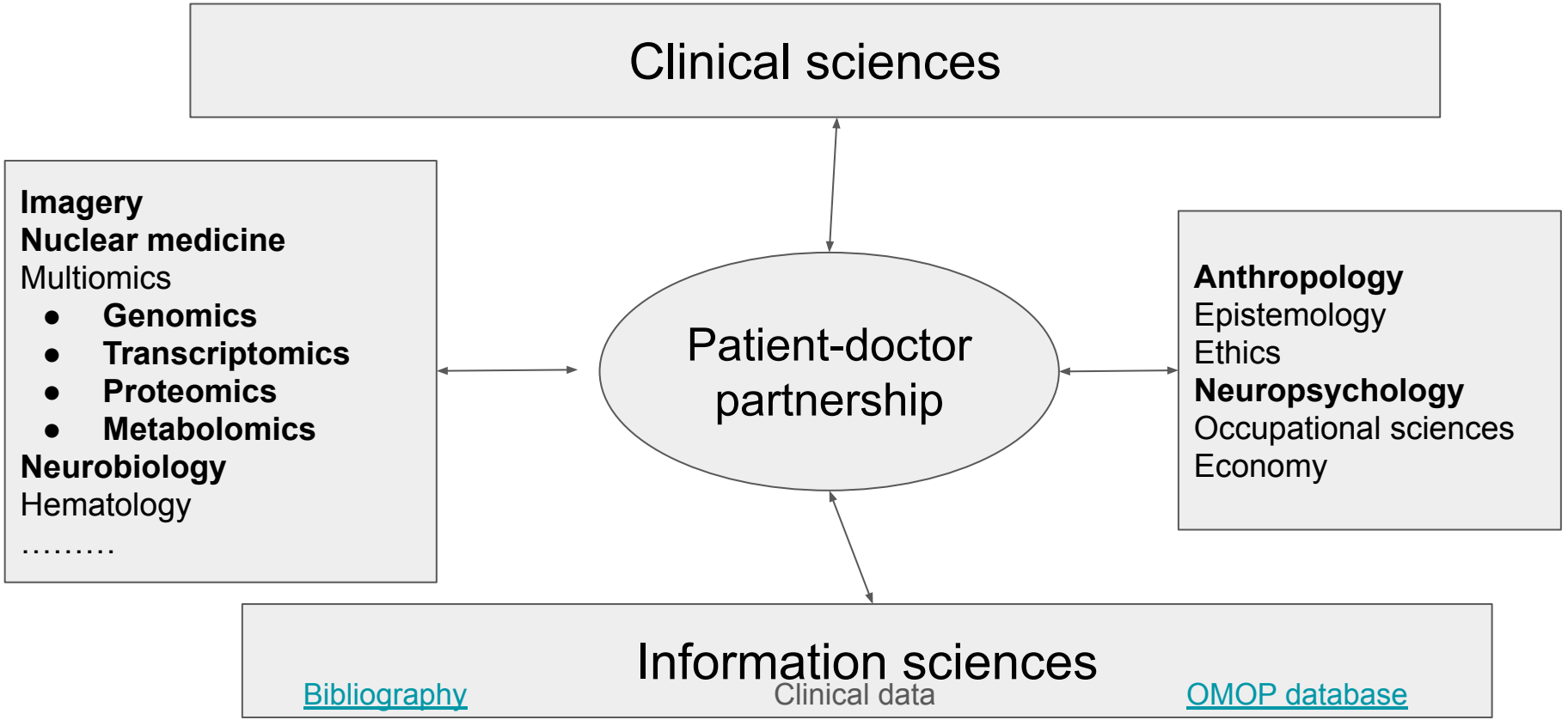
< 2020 Long Covid

Woman 72. Interview recorded, analysed by CHATGPT4o.

Symptom	HPO	ICPC-2	SNOMED CT
Chronic fatigue (1990-2020)	Chronic fatigue (HP:0012378)	A04 - Weakness/tiredness	84229001 - Fatigue
Worsened fatigue (Post-2020)	Severe fatigue (HP:0012436)	A04 - Weakness/tiredness	84229001 - Fatigue
Musculoskeletal pain (1990-2020)	Generalized muscle pain (HP:0031835)	L18 - Muscular pain	279039007 - Myalgia
Fluctuating pain	Episodic muscle weakness (HP:0003738)	L18 - Muscular pain	279039007 - Myalgia
Mild memory loss (1990-2020)	Mild cognitive impairment (HP:0001442)	P20 - Memory disturbance	386807006 - Mild memory impairment
Concentration difficulties	Attention deficit (HP:0000736)	P20 - Memory disturbance	162702000 - Reduced concentration
Sleep disturbances (1990-2020)	Sleep disturbance (HP:0002360)	P06 - Sleep disorder	106126000 - Sleep disorder
Worsened sleep disturbances (Post-2020)	Nightmare disorder (HP:0002363)	P06 - Sleep disorder	54329005 - Sleep disturbance due to dreams
Effort intolerance (1990-2020)	Exercise intolerance (HP:0003546)	A04 - Weakness/tiredness	23914001 - Reduced exercise tolerance
Autonomy preserved (1990-2020)	Mild limitation of activity (HP:0031792)	A28 - Limited function/daily life	16252002 - Limited functional autonomy
Tremors (Post-2020)	Tremor (HP:0001337)	N03 - Tremor	26079004 - Tremor
Disorientation (Post-2020)	Disorientation (HP:0001289)	P70 - Confusion	40917007 - Disorientation
Worsened cognitive issues (Post-2020)	Severe cognitive impairment (HP:0011446)	P20 - Memory disturbance	386807006 - Cognitive impairment
Vertigo (Post-2020)	Vertigo (HP:0002321)	N17 - Vertigo/dizziness	399144002 - Vertigo
Dysautonomia (Post-2020)	Dysautonomia (HP:0011036)	K88 - Hypotension orthostatic	17338001 - Dysautonomia
Respiratory symptoms (Post-2020)	Dyspnea on exertion (HP:0002873)	R02 - Shortness of breath	267036007 - Dyspnea
Reduced autonomy (Post-2020)	Severe limitation of activity (HP:0003794)	A28 - Limited function/daily life	16252002 - Limited functional autonomy

Incredible opportunity to develop a multidisciplinary research from the primary care line

Family medicine is at the interface of the biosciences and the humanities.



abstract submitted Sept 20, 2024

Invisible disease, multidisciplinary answer: the need for a Belgian Long Covid Research Network

Jamoulle M [1] , Kazeneza-Mugisha G [3] , Schmitz O [4] , Soylu S [3] , Nicaise C [4] , Mignolet M [4] , Bulpa P [4] , Dosimont S [5] , Thielemans P [6] , Latignies O [3] , Van Weyenbergh J [7]

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2 University of Louvain (UCL), Brussels, Belgium
3 University of Brussels (ULB) , Brussels , Belgium
4 Université de Namur.(UNamur), Namur, Belgium
5 Haute École Louvain-en-Hainaut, Charleroi, Belgium
6 Epicura Hospital , Ath, Belgium
7 University of Leuven (KUL), Leuven, Belgium

Classification issues

Rouen MBA. Rome, portail

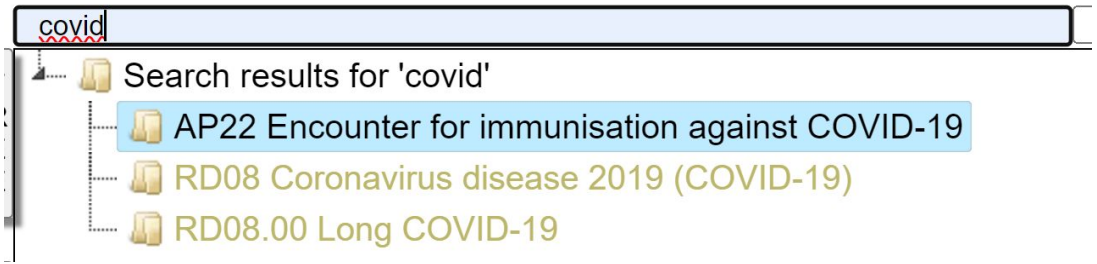
- Covid 19 is a viral disease
- Long Covid is a chronic viral disease
- Sars-Cov-2 concerns the whole human beings, physically, mentally and socially
- The entry point is not only respiratory
- Numerous symptoms were simply unknown by the patients & by the doctors
- The pattern of symptoms was also unknown
- ME/CSF and LC share enough characteristics to class them together
- ME/CFS patients are now included in our research

Prof. Iwasaki: Based on our data so far, immunological factors alone are able to classify people with long Covid vs. those who don't have long Covid with 94% accuracy. https://www.fresenius.com/This-is-a-tremendous-win-for-the-patients

Proposal

- AD General diagnoses and diseases
  - AD01 Measles
  - AD02 Chickenpox
  - AD03 Rubella
  - AD04 Infectious mononucleosis
  - AD05 Covid-19
  - AD06 Long Covid

reconsider



AS05.00 Chronic fatigue syndrome

Search terms
myalgic encephalomyelitis

ICPC-2
A04

ICPC-1NL
A04.01

SNOMED CT
chronic fatigue syndrome 52702003

immunological studies will probably reclassify ME/CSF as long term viral disease

Komaroff AL, Lipkin WI. ME/CFS and Long COVID share similar symptoms and biological abnormalitie
road map to the literature. *Frontiers in Medicine*. 2023;10. Accessed September 17, 2023.
https://www.frontiersin.org/articles/10.3389/fmed.2023.1187163

Publications

- Jamoulle M. (2021-2024) Open bibliography classified online on Long covid
- 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.
- Jamoulle, M. (2022). “Ca fait bizarre que quelqu'un m'écoute” Le long Covid en médecine de famille. ORBi-University of Liège
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- Jamoulle, M., & Van Weyenbergh, J. (2024). The Covid Resistance Study project - Start 2021- Update June 2024. ORBi-University of Liège.

J.Bosch 1500